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(54) Title: APOPTOSIS MODULATORS THAT INTERACT WITH THE HUNTINGTON'S DISEASE GENE

(57) Abstract

A family of proteins, including a specific human protein designated as HIP1, has been identified that interact differently with the gene product of a normal (16 CAG repeat) and an expanded (>44 CAG repeat) HD gene. Expression of the HIP1 protein was found to be enriched in the brain. Analysis of the sequence of the HIP1 protein indicated that it includes a death effector domain (DED), suggesting an apoptotic function. Thus, it appears that a normal function of Huntingtin may be to bind HIP1 and related apoptosis modulators, reducing its effectiveness in stimulating cell death. Since expanded huntingtin performs this function less well, there is an increase in HIP1–modulated cell death in individuals with an expanded repeat in the HD gene. This understanding of the likely role of huntingtin and HIP1 or related proteins (collectively "HIP–apoptosis modulating proteins") in the pathology of Huntington's disease offers several possibilities for therapy. First, because the function of huntingtin apparently depends at least in part on the ability to interact with HIP–apoptosis modulating proteins, added expression (e.g., via gene therapy) of normal (non–expanded) huntingtin or of the HIP–binding region of huntingtin should provide a therapeutic benefit. Other DED–interacting peptides could also be used to mask and reduce the interaction of HIP–apoptosis modulating proteins with the death signaling complex. Alternatively, a mutant form of HIP–protein from which the DED has been deleted might be introduced, for example using gene therapy techniques. Because HIP–apoptosis modulating proteins have been shown to self–associate, a protein with a deleted DED may compete with endogenous HIP–protein in the formation of these associations, thereby reducing the amount of apoptotically–active HIP–protein.

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APOPTOSIS MODULATORS THAT INTERACT WITH THE HUNTINGTON'S DISEASE GENE

BACKGROUND OF THE INVENTION

This application relates to a family of apoptosis modulators that interact with the Huntington's Disease gene product, and to methods and compositions relating thereto.

"Interacting proteins" are proteins which associate *in vivo* to form specific complexes. Non-covalent bonds, including hydrogen bonds, hydrophobic interactions and other molecular associations form between the proteins when two protein surfaces are matched or have affinity for each other. This affinity or match is required for the recognition of the two proteins, and the formation of an interaction. Protein-protein interactions are involved in the assembly of enzyme subunits; in antigen-antibody reactions; in forming the supramolecular structures of ribosomes, filaments, and viruses; in transport; and in the interaction of receptors on a cell with growth factors and hormones.

Huntington's disease is an adult onset disorder characterized by selective neuronal loss in discrete regions of the brain and spinal chord that lead to progressive movement disorder, personality change and intellectual decline. From onset, which generally occurs around age 40, the disease progresses with worsening symptoms, ending in death approximately 18 years after onset.

The biochemical cause of Huntington's disease is unclear. While the biochemical cause of Huntington's disease has remained elusive, a mutation in a gene within chromosome 4p16.3 subband has been identified and linked to the disease. This gene, referred to as the Huntington's Disease or HD gene, contains two repeat regions, a CAG repeat region and a CCG repeat region. Testing of Huntington's disease patients has shown that the CAG region is highly polymorphic, and that the number of CAG repeat units in the CAG repeat region is a very reliable indicator of having inherited the gene for Huntington's disease. Thus, in control individuals and in most individuals suffering from neuropsychiatric disorders other than Huntington's disease, the number of CAG repeats is between 9 and 35, while in individuals suffering from Huntington's disease the number of CAG repeats is expanded and is 36 or greater.

To date, no differences have been observed at either the total RNA, mRNA or protein levels between normal and HD-affected individuals. Thus, the function of the HD protein and its role in the pathogenesis of Huntington's Disease remain to be elucidated.

SUMMARY OF THE INVENTION

We have now identified a protein designated as HIP1, that interact differently with the gene product of a normal (16 CAG repeat) and an expanded (>44 CAG repeat) HD gene. The HIP1 protein originally isolated from a yeast two-hybrid screen is encoded by a 1.2 kb cDNA (Seq. ID. No. 1), devoid of stop codons, that is expressed as a 400 amino acid polypeptide (Seq. ID. No. 2). Subsequent study has elucidated additional sequence for HIP1 such that a 1090 amino acid protein is now known. (Seq. ID No. 5). Expression of the HIP1 protein was found to be enriched in the brain.

Analysis of the sequence of the HIP1 protein indicated that it includes a death effector domain (DED), suggesting an apoptotic function. Thus, it appears that a normal function of huntingtin may be to bind HIP1 and related apoptosis modulators, reducing its effectiveness in stimulating cell death. Since expanded huntingtin performs this function less well, there is an increase in HIP1-modulated cell death in individuals with an expanded repeat in the HD gene. Furthermore, additional members of the same family of proteins have been identified which also contain a DED. Thus, the present invention provides a new class of apoptotic modulators which are referred to as HIP-apoptosis modulating proteins.

This understanding of the likely role of huntingtin and HIP1 or related proteins in the pathology of Huntington's Disease offers several possibilities for therapy. First, because the function of huntingtin apparently depends at least in part on the ability to interact with HIP-apoptosis modulating proteins, added expression (e.g., via gene therapy) of normal (non-expanded) huntingtin or of the HIP-binding region of huntingtin should provide a therapeutic benefit. Other DED-interacting peptides could also be used to mask and reduce the interaction of HIP-apoptosis modulating proteins with the death signaling complex. Alternatively, a mutant form of HIP-protein from which the DED has been deleted might be introduced, for example using gene therapy techniques. Because HIP-apoptosis modulating proteins have been shown to self-associate, a protein with a deleted DED may compete with

endogenous HIP-protein in the formation of these associations, thereby reducing the amount of apoptotically-active HIP-protein.

BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 graphically depicts the amount of interaction between HIP1 and Huntingtin proteins with varying lengths of polyglutamine repeat;

Fig. 2 compares the nucleic acid sequences of human and murine HIP1 and HIP1a;

Fig. 3 compares the amino acid sequences of human and murine HIP1 and HIP1a;

Fig. 4 shows the sequences of various death effector domains in comparison to the DED of human and murine HIP1 and HIP1a;

Fig. 5 shows the genomic organization of human HIP1;

Fig. 6 compares the sequences of human HIP1 with ZK370.3 protein of *C. elegans*;

Fig. 7 shows mouse EST's with homology to human HIP1 cDNA used to screen a mouse brain library;

Fig. 8 shows the affect of HIP1 on susceptibility of cells to stress; and

Figs. 9A - 9C show the toxicity of HIP1 in the presence of huntingtin with different lengths of polyglutamine repeats.

DETAILED DESCRIPTION OF THE INVENTION

This application relates to a new family of proteins function as modulators of apoptosis. At least some of these proteins, notably the human protein designated HIP1, interact with the gene product of the Huntington's disease gene. Other proteins within the family possess at least 40% and preferably more than 50% nucleotide identity with HIP1 and include a death effector domain (DED) . Such proteins are referred to in the specification and claims hereof as "HIP-apoptosis modulating proteins."

The first HIP-apoptosis modulating protein identified was designated as HIP1. HIP1 was identified using the yeast two-hybrid system described in US Patent No. 5,283,173 which is incorporated herein by reference. Briefly, this system utilizes two chimeric genes or plasmids expressible in a yeast host. The yeast host is selected to contain a detectable marker gene having a binding site for the DNA binding domain of a transcriptional activator. The

first chimeric gene or plasmid encodes a DNA-binding domain which recognizes the binding site of the selectable marker gene and a test protein or protein fragment. The second chimeric gene or plasmid encodes for a second test protein and a transcriptional activation domain. The two chimeric genes or plasmids are introduced into the host cell and expressed, and the cells are cultivated. Expression of the detectable marker gene only occurs when the gene product of the first chimeric gene or plasmid binds to the DNA binding domain of the detectable marker gene, and a transcriptional activation domain is brought into sufficient proximity to the DNA-binding domain, an occurrence which is facilitated by protein-protein interactions between the first and second test proteins. By selecting for cells expressing the detectable marker gene, those cells which contain chimeric genes or plasmids for interacting proteins can be identified, and the gene can be recovered and identified.

In testing for Huntington Interacting Proteins, several different plasmids were prepared containing portions of the human HD gene. The first four, identified as 16pGBT9, 44pGBT9, 80pGBT9 and 128pGBT9, were GAL4 DNA binding domain-HD in-frame fusions containing nucleotides 314 to 1955 (amino acids 1-540) of the published HD cDNA sequences cloned into the vector pGBT9 (Clontech). These plasmids contain a CAG repeat region of 16, 44, 80 and 128 glutamine-encoding repeats, respectively. A clone (DMK BamHIpGBT9) was made by fusing a cDNA encoding the first 544 amino acids of the myotonic dystrophy gene (a gift from R. Korneluk) in-frame with the GAL4-DNA BD of pGBT9 and was used as a negative control.

These plasmids have been used to identify and characterize HIP1, as well as two additional HD-interacting proteins, HIP2 and HIP3, which have not yet been tested for function as apoptosis modulators. These plasmids can be further used for the identification of additional interacting proteins which do act as apoptosis modulators, and for tests to refine the region on the protein in which the interaction occurs. Thus, one aspect of the invention is these four plasmids, and the use of these plasmids in identifying HD-interacting proteins. Furthermore, it will be appreciated that the GAL4 DNA-binding and activating domains are not the only domains which can be used in the yeast two-hybrid assay. Thus, in a broader sense, the invention encompasses any chimeric genes or plasmids containing nucleotides 314 to 1955 of the HD gene together with an activating or DNA-binding domain suitable for use

in the yeast one, two- or three-hybrid assay for proteins critical in either binding to the HD protein or responsible for regulated expression of the HD gene.

After introducing the plasmids into Y190 yeast host cells, transforming the host cells with an adult human brain Matchmaker™ (Clontech) cDNA library coupled with a GAL4 activating domain, and selecting for the expression of two detectable marker genes to identify clones containing genes for interacting proteins, the activating domain plasmids were recovered and analyzed. As a result of this analysis, three different cDNA fragments were identified as encoding for HD-interacting proteins and designated as HIP1, HIP2 and HIP3. The nucleic acid sequence of HIP1, as originally recovered in the yeast two-hybrid assay, is given in Seq. ID. No 1. The polypeptide which it encodes is given by Seq. ID No. 2. Further investigation of the HIP1 cDNA resulted in the characterization of a longer region of cDNA totaling 4795 bases and a corresponding protein, the sequences of which are given by Seq ID Nos. 3 and 4, respectively. A further portion of the HIP1 protein was characterized, extending the length to the complete protein sequence of 1090 amino acids (Seq. ID No. 5)

The cDNA molecules encoding HIP-apoptosis modulating proteins, particularly those encoding portions of HIP1, can be explored using oligonucleotide probes for example for amplification and sequencing. In addition, oligonucleotide probes complementary to the cDNA can be used as diagnostic probes to localize and quantify the presence of HIP1 DNA. Probes of this type with a one or two base mismatch can also be used in site-directed mutagenesis to introduce variations into the HIP1 sequence which may increase or decrease the apoptotic activity. Preferred targets for such mutations would be the death effector domains. Thus, a further aspect of the present invention is an oligonucleotide probe, preferably having a length of from 15-40 bases which specifically and selectively hybridizes with the cDNA given by Seq. ID No. 1 or 3 or a sequence complementary thereto. As used herein, the phrase "specifically and selectively hybridizes with" the cDNA refers to primers which will hybridize with the cDNA under stringent hybridization conditions.

Probes of this type can also be used for diagnostic purposes to characterize risk of Huntington's Disease like symptoms arising in individuals where the symptoms are present in the family history but are not associated with an expansion of the CAG repeat. Such symptoms may arise from a mutation in HIP1 or other HIP-apoptosis modulating protein

which alters the interaction of this protein with huntingtin, thereby increasing the apoptotic activity of the protein even in the presence of a normal (non-expanded) huntingtin molecule. An appropriate probe for this purpose would one which hybridizes with or adjacent to the huntingtin binding region of the HIP-apoptosis modulating protein. In HIP1, this lies within amino acids 129-514.

DNA sequencing of the HIP1 cDNA initially isolated from the yeast two-hybrid screen (Seq. ID No. 1) revealed a 1.2 kb cDNA that shows no significant degree of nucleic acid identity with any stretch of DNA using the blastn program at ncbi (blast@ncbi.nlm.nih.gov). When the larger HIP1 cDNA sequence (SEQ ID NO. 3) was translated into a polypeptide, the HIP1 cDNA coding (nucleotides 328-3069) is observed to be devoid of stop codons, and to produce a 914 amino acid polypeptide. A polypeptide identity search revealed an identity match over the entire length of the protein (46% conservation) with that of a hypothetical protein from *C. elegans* (ZK370.3 protein; *C. elegans* cosmid ZK370). This *C. elegans* protein shares identity with the mouse talin gene, which encodes a 217 kDa protein implicated with maintaining integrity of the cytoskeleton. It also shares identity with the SLA2/MOP2/ END4 gene from *Saccharomyces cerevisiae*, which is known to code for an essential cytoskeletal associated gene required for the accumulation and or maintenance of plasma membrane H^+- ATPase on the cell surface. When pairwise comparisons are performed between HIP1 and the C. elegans ZK370.3 protein (Genpept accession number celzk370.3), it shows 26% complete identity and an overall 46% level of conservation. Comparative analysis between HIP1 and SLA2/MOP2/ END4 (EMBL accession number Z22811) demonstrate similar conservation (20% identity, 40% conservation).

Further exploration revealed several important facts about HIP1 that implicate it in a significantly in the pathogenesis of Huntington's Disease. First, as shown in Fig. 1, it was found that the native interaction between HD protein and HIP1 is influenced by the number of CAG repeats. Second, it was found that expression of the HIP1 protein is enriched in the brain. The highest amounts of expression are in the cortex, with lower levels being seen in the cerebellum, caudate and putamen.

It has also been observed that huntingtin proteins with expanded polyglutamine tracts can aggregate into large, irregularly shaped deposits in HD brains, transgenic mice and *in vitro* cell culture. We have shown that in HEK (human embryonic kidney) 293T cells, the aggregation of full-length and smaller huntingtin fragments occurs after the cells have been exposed to a period of apoptotic stress. Martindale, et al., *Nature Genetics* 18: 150-154 (1998). In order to assess the consequence of HIP1 expression in cultured cells, we used huntingtin aggregation as one marker of viability. What we found was that cells cotransfected with huntingtin (128 CAG repeats) and HIP1 contained aggregates comparable to those observed following application of apoptotic stress with sub-lethal doses of tamoxifen in 14% of the cells, and that these cells were the ones in which both genes had been introduced as reflected by a double marker experiment. Transfection of a gene encoding a fusion protein of 128 repeat huntingtin and the DED domain from HIP1 ligated in the sense orientation resulted in aggregate formation in 30 to 50% of the cells.

The implications of the apoptotic activity of HIP1 are two-fold. First, the fact that this activity is apparently differentially modulated by interaction with huntingtin having normal and expanded repeats implicates HIP1 in the apoptotic neuronal death which is observed in Huntington's disease and makes HIP1 a logical target for therapy. A second implication of the apoptotic activity of HIP1 is the potential for use of HIP1 as a therapeutic agent to introduce apoptosis in cancer cells.

Therapeutic targeting of HIP1 or other HIP-apoptosis modulating proteins might take any of several forms, but will in general be a treatment involving administration of a composition that reduces the apoptotic activity of the HIP-apoptosis modulating protein. As used in the specification and claims hereof, the term "administration" includes direct administration of a composition active to reduce apoptotic activity as well as indirect administration which might include administration of pro-drugs or nucleic acids that encode the desired therapeutic composition.

One class of composition which can be used in the therapeutic methods of the invention are those compositions which interfere with the activity of HIP-apoptosis modulating proteins by binding to the proteins and mask and reduce the interaction of HIP-apoptosis modulating proteins with the death signaling complex. Within this class of

compositions are normal (non-expanded) huntingtin, administered, for example, via increased expression of exogenous HD genes; the HIP-binding region of huntingtin, administered via gene therapy techniques; and other DED-interacting peptides. Other DED-interacting peptides which might be used in a therapeutic method of this type include FADD (Beldin et al., *Cell* 85: 803-815 (1996)) and caspase 8 (Muzio et al., *Cell* 85: 817-827 (1996).

An alternative form of therapy involves the use of a mutant form of HIP1 or other HIP-apoptosis modulating protein from which the DED has been deleted. DED-containing proteins, including HIP1 are self-associating, and this self-association has been shown to be important for activity. (Muzio et al., *Cell* 85: 817-827 (1996). Thus, a protein with a deleted DED may compete with endogenous HIP-protein in the formation of these associations, thereby reducing the amount of apoptotically-active HIP-protein.

In addition to HIP1, we have identified a further human protein, HIP1a, from a human frontal cortex cDNA library. HIP1a is a family member of HIP1, and thus a HIP-apoptosis modulator in accordance with the invention. A partial sequence of HIP1a (the 5' portion of HIP1a remains to be characterized) is given by SEQ ID Nos. 6 and 7. The isolated and characterized portion of HIP1a shows 53% nucleotide identity and 58% amino acid conservation with HIP1 (Table 1, Figs. 2 and 3).

We have also isolated 2 mouse proteins mHIP1 and mHIP1a (SEQ. ID Nos. 8-11) which appear to be the murine homologues of human HIP1 and HIP1a. As in the case of human HIP1a, the 5' portion of mHIP1 remains to be isolated. At present, mHIP1 shows 85% nucleotide identity and 90% amino acid conservation with huHIP1 (Table 1, Figs. 2 and 3). mHIP1a shows 60% nucleotide identity and 61% amino acid conservation with huHIP1 (Table 1, Figs. 2 and 3). mHIP1a shows stronger homology to huHIP1a; it shows 87% nucleotide identity and 91% amino acid conservation with huHIP1a (Table 1, Figs. 2 and 3). Taken together these findings indicate that mHIP1 is the murine homologue of huHIP1 whereas mHIP1a is most likely the murine homologue of huHIP1a. As mentioned previously, HIP1 shows sequence similarity to Sla2p in S. cerevisiae and the hypothetical protein ZK370.3 in C. elegans. Similarly, huHIP1a, mHIP1, and mHIP1a show sequence similar to Sla2p and ZK370.3 (Table 2). The carboxy-terminal regions of huHIP1a, mHIP1, and mHIP1a all show considerable homology to the mammalian membrane

cytoskeletal-associated protein, talin. This suggests that these 3 proteins may also play a role in the regulation of membrane events through interactions with the underlying cytoskeleton.

HIP1 contains a death effector domain (DED), a domain which is also present in a number of proteins involved in the apoptotic pathway (Fig. 4). This suggests that HIP1 may act as a modulator of the apoptosis pathway. The DED in huHIP1 is present between amino acid positions 287 and 368. Similarly, HIP1a, mHIP1, and mHIP1a also contain a DED. In huHIP1a the DED is present at amino acids 1-78 of the recovered fragment. In mHIP1 and mHIP1a, the DED are present at amino acids 128- 210 and 388-470, respectively. The DED present in huHIP1a, mHIP1 and mHIP1a all show significant percentage amino acid conservation to the DED present in huHIP1 (Table 3).

Increasing expression of normal (non-expanded) huntingtin or the HIP-apoptotic modulator-binding portion thereof, a modified HIP-apoptotic modulator in which the DED has been deleted or of a DED-interacting protein or peptide can be accomplished using gene therapy approaches. In general, this will involve introduction of DNA encoding the appropriate protein or peptide in an expressable vector into the brain cells. Expression of HIP-apoptosis modulating proteins may also be useful in treatment of cancer in which case application to other cell types would be desired, and cells expressing HIP-apoptosis modulating proteins may be used for screening of therapeutic compounds. Thus, in a more general sense, expression vectors are defined herein as DNA sequences that are required for the transcription of cloned copies of genes and the translation of their mRNAs in an appropriate cell type. Specifically designed vectors allow the shuttling of DNA between hosts such as bacteria-yeast or bacteria-animal cells. An appropriately constructed expression vector may contain: an origin of replication for autonomous replication in host cells, selectable markers, a limited number of useful restriction enzyme sites, a potential for high copy number, and active promoters. A promoter is defined as a DNA sequence that directs RNA polymerase to bind to DNA and initiate RNA synthesis. A strong promoter is one which causes mRNAs to be initiated at high frequency. Expression vectors may include, but are not limited to, cloning vectors, modified cloning vectors, specifically designed plasmids or viruses.

A variety of mammalian expression vectors may be used to express recombinant

HIP-apoptosis modulating proteins or fragments thereof in mammalian cells. Commercially available mammalian expression vectors which may be suitable for recombinant HIP-apoptosis modulating protein expression, include but are not limited to, pMC1neo (Stratagene), pXT1 (Stratagene), pSG5 (Stratagene), EBO-pSV2-neo (ATCC 37593) pBPV-1(8-2) (ATCC 37110), pdBPV-MMTneo(342-12) (ATCC 37224), pRSVgpt (ATCC 37199), pRSVneo (ATCC 37198), pSV2-dhfr (ATCC 37146), pUCTag (ATCC 37460), and lZD35 (ATCC 37565). Other vectors which have been shown to be suitable expression systems in mammalian cells include the herpes simplex viral based vectors: pHSV1 (Geller et al. Proc. Natl. Acad. Sci 87:8950-8954 (1990)); recombinant retroviral vectors: MFG (Jaffee et al. Cancer Res. 53:2221-2226 (1993)); Moloney-based retroviral vectors: LN, LNSX, LNCX, LXSN (Miller and Rosman Biotechniques 7:980-989 (1989)); vaccinia viral vector: MVA (Sutter and Moss Proc. Natl. Acad. Sci. 89:10847-10851 (1992)); recombinant adenovirus vectors : pJM17 (Ali et al Gene Therapy 1:367-384 (1994)), (Berkner K. L. Biotechniques 6:616-624 1988); second generation adenovirus vector: DE1/DE4 adenoviral vectors (Wang and Finer Nature Medicine 2:714-716 (1996)); and Adeno-associated viral vectors: AAV/Neo (Muro-Cacho et al. J. Immunotherapy 11:231-237 (1992)).

The expression vector may be introduced into host cells via any one of a number of techniques including but not limited to transformation, transfection, infection, protoplast fusion, and electroporation. The expression vector-containing cells are clonally propagated and individually analyzed to determine whether they produce the desired protein. Delivery of retroviral vectors to brain and nervous system tissue has been described in US Patents Nos. 4,866,042, 5,082,670 and 5,529,774, which are incorporated herein by references. These patents disclose the use of cerebral grafts or implants as one mechanism for introducing vectors bearing therapeutic gene sequences into the brain, as well as an approach in which the vectors are transmitted across the blood brain barrier.

To further illustrate the methods of making the materials which are the subject of this invention, and the testing which has established their utility, the following non-limiting experimental procedures are provided.

EXAMPLE 1

IDENTIFICATION OF INTERACTING PROTEINS

GAL4-HD cDNA constructs

An HD cDNA construct (44pGBT9), with 44 CAG repeats was generated encompassing amino acids 1 - 540 of the published HD cDNA . This cDNA fragment was fused in frame to the GAL4 DNA-binding domain (BD) of the yeast two-hybrid vector pGBT9 (Clontech). Other HD cDNA constructs, 16pGBT9, 80pGBT9 and 128pGBT9 were constructed, identical to 44pGBT9 but included only 16, 80 or 128 CAG repeats, respectively.

Another clone (DMKDBamHIpGBT9) containing the first 544 amino acids of the myotonic dystrophy gene (a gift from R. Korneluk) was fused in-frame with the GAL4-DNA BD of pGBT9 and was used as a negative control. Plasmids expressing the GAL4-BDRAD7 (D. Gietz, unpublished) and SIR3 were used as a positive control for the β-galactosidase filter assay.

The clones IT15-23Q, IT15-44Q and HAP1 were generous gifts from Dr. C. Ross. These clones represent a previously isolated huntingtin interacting protein that has a higher affinity for the expanded form of the HD protein.

Yeast strains, transformations and β-galactosidase assays

The yeast strain Y190 (MATa leu2-3,112, ura3-52, trp1-901, his3-Δ200, ade2-101, gal4Δgal80Δ, URA3::GAL-lacZ, LYS2::GAL-HIS3,cyc^r) was used for all transformations and assays. Yeast transformations were performed using a modified lithium acetate transformation protocol and grown at 30 C using appropriate synthetic complete (SC) dropout media.

The β-galactosidase chromogenic filter assays were performed by transferring the yeast colonies onto Whatman filters. The yeast cells were lysed by submerging the filters in liquid nitrogen for 15-20 seconds. Filters were allowed to dry at room temperature for at least five minutes and placed onto filter paper presoaked in Z-buffer (100 mM sodium phosphate (pH7.0) 10 mM KCl, 1 mM $MgSO_4$) supplemented with 50 mM

2-mercaptoethanol and 0.07 mg/ml 5-bromo-4-chloro-3-indolyl β-D-galactoside (X-gal). Filters were placed at 37 C for up to 8 hours.

Yeast two-hybrid screening for huntingtin interacting protein (HIP)

cDNAs from an human adult brain Matchmaker™ cDNA library (Clontech) was transformed into the yeast strain Y190 already harboring the 44pGBT9 construct. The transformants were plated onto one hundred 150 mm x 15 mm circular culture dishes containing SC media deficient in Trp, Leu and His. The herbicide 3-amino-triazole (3-AT) (25mM) was utilized to limit the number of false His+ positives (31). The yeast transformants were placed at 30 C for 5 days and β-galactosidase filter assays were performed on all colonies found after this time, as described above, to identify β-galactosidase+ clones. Primary His+/β-galactosidase+ clones were then orderly patched onto a grid on SC -Trp/-Leu/-His (25 mM 3AT) plates and assayed again for His+ growth and the ability to turn blue with a filter assay. Secondary positives were identified for further analysis. Proteins encoded by positive cDNAs were designated as HIPs (Huntingtin Interactive Proteins). Approximately 4.0 x 10^7 Trp/Leu auxotrophic transformants were screened and of 14 clones isolated 12 represented the same cDNA (HIP1), and the other 2 cDNAs, HIP2 and HIP3 were each represented only once.

The HIP cDNA plasmids were isolated by growing the His+/β-galactosidase+ colony in SC -Leu media overnight, lysing the cells with acid-washed glass beads and electroporating the bacterial strain, KC8 (leuB auxotrophic) with the yeast lysate. The KC8 ampicillin resistant colonies were replica plated onto M9 (-Leu) plates. The plasmid DNA from M9+ colonies was transformed into DH5-a for further manipulation.

EXAMPLE 2

CONFIRMATION OF INTERACTIONS

The HIP1-GAL4-AD cDNA activated both the lac-Z and His reporter genes in the yeast strain Y190 only when co-transformed with the GAL4-BD-HD construct, but not the negative controls (Fig. 1) of the vector alone or a random fusion protein of the myotonin kinase gene. In order to assess the influence of the polyglutamine tract on the interaction

between HIP1 and HD, semi-quantitative β-galactosidase assays were performed. GAL4-BD-HD fusion proteins with 16, 44, 80 and 128 glutamine repeats were assayed for their strength of interaction with the GAL4-AD-HIP1 fusion protein.

Liquid β-galactosidase assays were performed by inoculating a single yeast colony into appropriate synthetic complete (SC) dropout media and grown to OD600 0.6-1.5. Five millilitres of overnight culture was pelleted and washed once with 1 ml of Z-Buffer, then resuspended in 100 ml Z-Buffer supplemented with 38 mM 2-mercaptoethanol, and 0.05% SDS. Acid washed glass beads (~100 ml) were added to each sample and vortexed for four minutes, by repeatedly alternating a 30 seconds vortex, with 30 seconds on ice. Each sample was pelleted and 10 ml of lysate was added to 500 ml of lysis buffer. The samples were incubated in a 30 C waterbath for 30 seconds and then 100 ml of a 4 mg/ml o-nitrophenyl b-D galactopyranoside (ONPG) solution was added to each tube. The reaction was allowed to continue for 20 minutes at 30 C and stopped by the addition of 500 ml of 1 M Na_2CO_3 and placing the samples on ice. Subsequently, OD420 was taken in order to calculate the β-galactosidase activity with the equation 1000 x OD420/(t x V x OD600) where t is the elapsed time (minutes) and V is the amount of lysate used.

The specificity of the HIP1-HD interaction can be observed using the chromogenic filter assay. Only yeast cells harboring HIP1 and HD activate both the HIS and lacZ reporter genes in the Y190 yeast host. The cells that contain the HIP1 with HD constructs with 80 or 128 CAG repeats turn blue approximately 45 minutes after the cells with the smaller sized repeats (16 or 44).

No difference in the β-galactosidase activity was observed between the 16 and 44 repeats or between the 80 and 128 repeats. However, a significant difference ($p<0.05$) in activity is seen between the smaller repeats (16 and 44) and the larger repeats (80 and 128). (Figure 1)

EXAMPLE 3

DNA SEQUENCING, cDNA ISOLATION AND 5' RACE

Oligonucleotide primers were synthesized on an ABI PCR-mate oligo-synthesizer. DNA sequencing was performed using an ABI 373 fluorescent automated DNA sequencer.

The HIP cDNAs were confirmed to be in-frame with the GAL4-AD by sequencing across the AD-HIP1 cloning junction using an AD oligonucleotide (5'GAA GAT ACC CCA CCA AAC3'). (Seq. ID No. 12)

Subsequently, primer walking was used to determine the remaining sequences. A human frontal cortex >4.0 kb cDNA library (a gift from S. Montal) was screened to isolate the full length HIP1 gene. Fifty nanograms of a 558 base pair Eco RI fragment from the original HIP1 cDNA was radioactively labeled with [α^{32}P]-dCTP using nick-translation and the probe allowed to hybridized to filters containing >105 pfu/ml of the cDNA library overnight at 65°C in Church buffer (see Northern blot protocol). The filters were washed at 65°C for 10 minutes with 1 X SSPE, 15 minutes at 65 C with 1 X SSPE and 0.1% SDS, then for thirty minutes and fifteen minutes with 1 X SSPE and 0.1% SDS. The filters were exposed to X-ray film (Kodak, XAR5) overnight at -70 C. Primary positives were isolated and replated and subsequent secondary positives were hybridized and washed as for the primary screen. The resulting positive phage were converted into plasmid DNA by conventional methods (Stratagene) and the cDNA isolated and sequenced.

In order to obtain the most 5' sequence of the HIP1 gene, a Rapid Amplification of cDNA Ends (RACE) protocol was performed according to the manufacturers recommendations (BRL). First strand cDNA was synthesized using the oligo HIP1-242R (5' GCT TGA CAG TGT AGT CAT AAA GGT GGC TGC AGT CC 3'). (Seq. ID No. 13) After dCTP tailing the cDNA with terminal deoxy transferase, two rounds of 35 cycles (94°C 1 minute; 53°C 1 minute; 72°C 2 minutes) of PCR using HIP1-R2 (5' GGA CAT GTC CAG GGA GTT GAA TAC 3') (Seq. ID No. 14) and an anchor primer (5' (CUA)4 GGC CAC GCG TCG ACT AGT ACG GGI IGG GII GGG IIG3') (BRL ,Seq. ID No. 15)) were performed. The subsequent 650 base pair PCR product was cloned using the TA cloning system (Invitrogen) and sequenced using T3 and T7 primers. Sequences ID Nos. 1 and 3 show the sequence of the HIP1 cDNAs obtained.

EXAMPLE 4

DNA AND AMINO ACID ANALYSES

Overlapping DNA sequence was assembled using the program MacVector and sent via email or Netscape to the BLAST server at NIH (http://www.ncbi.nlm.nih.gov) to search for sequence similarities with known DNA (blastn) or protein (tblastn) sequences. Amino acid alignments were performed with the program Clustalw.

EXAMPLE 5

FISH DETECTION SYSTEM AND IMAGE ANALYSIS

The HIP1 cDNA isolated from the two-hybrid screen was mapped by fluorescent in situ hybridization (FISH) to normal human lymphocyte chromosomes counterstained with propidium iodide and DAPI. Biotinylated probe was detected with avidin-fluorescein isothiocyanate (FITC). Images of metaphase preparations were captured by a thermoelectrically cooled charge coupled camera (Photometrics). Separate images of DAPI banded chromosomes and FITC targeted chromosomes were obtained. Hybridization signals were acquired and merged using image analysis software and pseudo colored blue (DAPI) and yellow (FITC) as described and overlaid electronically. This study showed that HIP1 maps to a single genomic locus at 7q11.2.

EXAMPLE 6

NORTHERN BLOT ANALYSIS

RNA was isolated using the single step method of homogenization in guanidinium isothiocyante and fractionated on a 1.0% agarose gel containing 0.6 M formaldehyde. The RNA was transferred to a hybond N -membrane (Amersham) and crosslinked with ultraviolet radiation.

Hybridization of the Northern blot with b-actin as an internal control probe provided confirmation that the RNA was intact and had transferred. The 1.2 kb HIP1 cDNA was labeled using nick translation and incorporation of α^{32}P-dCTP. Hybridization of the original 1.2 kb HIP1 cDNA was carried out in Church buffer (0.5 M sodium phosphate buffer, pH 7.2, 2.7% sodium dodecyl sulphate, 1 mM EDTA) at 55 C overnight. Following

hybridization, Northern blots were washed once for 10 minutes in 2.0 X SSPE, 0.1% SDS at room temperature and twice for 10 minutes in 0.15 X SSPE, 0.1% SDS. Autoradiography was carried our from one to three days using Hyperfilm (Amersham) film at -70 C.

Analysis of the levels of RNA levels of HIP1 by Northern blot data revealed that the 10 kilo base HIP1 message is present in all tissue assessed. However, the levels of RNA are not uniform, with brain having highest levels of expression and peripheral tissues having less message. No apparent differences in RNA expression was noted between control samples and HD affected individuals.

EXAMPLE 7

TISSUE LOCALIZATION OF HIP1

Tissue localization of HIP1 was studied using a variety of techniques as described below. Subcellular distribution of HIP-1 protein in adult human and mouse brain Biochemical fractionation studies revealed the HIP1 protein was found to be a membrane-associated protein. No immunoreactivity was seen by Western blotting in cytosolic fractions, using the anti-HIP1-pep1 polyclonal antibody. HIP1 immunoreactivity was observed in all membrane fractions including nuclei (P1), mitochondria and synaptosomes (P2), microsomes and plasma membranes (P3). The P3 fraction contained the most HIP1 compared to other membrane fractions. HIP1 could be removed from membranes by high salt (0.5M NaCl) buffers indicating it is not an integral membrane protein, however, since low salt (0.1- 0.25M NaCl) was only able to partially remove HIP1 from membranes, its membrane association is relatively strong. The extraction of P3 membranes with the non-ionic detergent, Triton X-100 revealed HIP1 to be a Triton X-100 insoluble protein. This characteristic is shared by many cytoskeletal and cytoskeletal-associated membrane proteins including actin, which was used as a control in this study. The biochemical characteristics of HIP1 described were found to be identical in mouse and human brain and was the same for both forms of the protein (both bands of the HIP1 doublet). HIP1 co-localized with huntingtin in the P2 and P3 membrane fractions, including the high-salt membrane extractions, as well as in the Triton X-100 insoluble residue. The subcellular distribution of HIP1 was unaffected by the

expression of polyglutamine-expanded huntingtin in transgenic mice and HD patient brain samples.

The localization of HIP1 protein was further investigated by immunohistochemistry in normal adult mouse brain tissue. Immunoreactivity was seen in a patchy, reticular pattern in the cytoplasm, appeared excluded from the nucleus and stained most intensely in a discontinuous pattern at the membrane. These results are consistent with the association of HIP1 with the cytoskeletal matrix and further indicate an enrichment of HIP1 at plasma membranes. Immunoreactivity occurred in all regions of the brain, including cortex, striatum, cerebellum and brainstem, but appeared most strongly in neurons and especially in cortical neurons. As described previously, huntingtin immunoreactivity was seen exclusively and uniformly in the cytosol.

The in situ hybridization studies showed HIP1 mRNA to be ubiquitously and generally expressed throughout the brain. This data is consistent with the immunohistochemical results and was identical to the distribution pattern of huntingtin mRNA in transgenic mouse brains expressing full-length human huntingtin.

Protein Preparation And Western Blotting For Expression Studies

Frozen human tissues were homogenized using a Polytron in a buffer containing 0.25M sucrose, 20mM Tris-HCl (pH 7.5), 10mM EGTA, 2mM EDTA supplemented with 10ug/ml of leupeptin, soybean trypsin inhibitor and 1mM PMSF, then centrifuged at 4,000rpm for 10' at 4 C to remove cellular debris. 100-150ug/lane of protein was separated on 8% SDS-PAGE mini-gels and then transferred to PVDF membranes. Huntingtin and HIP1 were electroblotted overnight in Towbin's transfer buffer (25 mM Tris-HCl, 0.192M glycine, pH8.3, 10% methanol) at 30V onto PVDF membranes (Immobilon-P, Millipore) as described (Towbin et al, *Proc. Nat'l Acad. Sci.(USA)* 76: 4350-4354 (1979)). Membranes were blocked for 1 hour at room temperature in 5% skim milk/ TBS (10mM Tris-HCl, 0.15M NaCl, pH7.5). Antibodies against huntingtin (pAb BKP1, 1:500), actin (mAb A-4700, Sigma, 1:500) or HIP1 (pAb HIP-pep1, 1:200) were added to blocking solution for 1 hour at room temperature. After 3 x 10 minutes washes in TBS-T (0.05% Tween-20/TBS), secondary Ab (horseradish peroxidase conjugated IgG, Biorad) was applied in blocking solution for 1 hour

at room temperature. Membranes were washed and then incubated in chemiluminescent ECL solution and visualized using Hyperfilm-ECL film (Amersham).

Generation of Antibodies

The generation of huntingtin specific antibodies GHM1 and BKP1 is described elsewhere (Kalchman, et al., *J. Biol. Chem.* 271: 19385-19394 (1996)). The HIP1 peptide (VLEKDDLMDMDASQQN, a.a. 76-91 of Seq. ID No. 2) was synthesized with Cys on the N-terminus for the coupling, and coupled to Keyhole limpet hemocyanin (KLH) (Pierce) with succinimidyl 4-(N-maleimidomethyl) cyclohexame-1-carboxylate (Pierce). Female New Zealand White rabbits were injected with HIP1 peptide-KLH and Freund's adjuvant. Antibodies against the HIP1 peptide were purified from rabbit sera using affinity column with low pH elution. Affinity column was made by incubation of HIP1 peptide with activated thio-Sepharose (Pharmacia).

Western blotting of various peripheral and brain tissues were consistent with the RNA data. The HIP1 protein levels observed was not equivalent in all tissues. The protein expression is predominant in brain tissue, with highest amounts seen in the cortex and lower levels seen in the cerebellum and caudate and putamen.

More regio-specific analysis of HIP1 expression in the brain revealed no differential expression pattern in affected individuals when compared to normal controls, with highest levels of expression seen in both controls and HD patients in the cortical regions.

EXAMPLE 8

CO-IMMUNOPRECIPITATION OF HIP1 WITH HUNTINGTIN

Confirmation of the HD-HIP1 interaction was performed using coimmunoprepitation as follows. Control human brain (frontal cortex) lysate was prepared in the same manner as for subcellular localization study. Prior to immunoprecipitation, tissue lysate was centrifuged at 5000 rpm for 2 minutes at 4 C, then the supernatant was pre-cleared by the incubated with excess amount of Protein A-Sepharose for 30 minutes at 4°C, and centrifuged at the same condition. Fifty microlitres of supernatant (500 mg protein) was incubated with or without antibodies (10 ug of anti-huntingtin GHM1 (Kalchman, et al. 1996) or anti-synaptobrevin antibody) in the total 500 ul of incubation buffer (20mM Tris-Cl

(pH7.5), 40mM NaCl, 1mM $MgCl_2$) for 1 hour at 4°C. Twenty microlitres of Protein A-Sepharose (1:1 suspension, for GHM1 and no antibody control) or Protein G-Sepharose (for anti-synaptobrevin antibody; Pharmacia) was added and incubated for 1 hour at 4°C. The beads were washed with washing buffer (incubation buffer containing 0.5 % Triton X-100) three times. The samples on the beads were separated using SDS-PAGE (7.5% acrylamide) and transferred to PVDF membrane (Immobilon-P, Millipore). The membrane was cut at about 150 kDa after transfer for Western blotting (as described above). The upper piece was probed with anti-huntingtin BKP1 (1/1000) and lower piece with anti-HIP1 antibody (1/300).

The results showed that when an anti-HIP1 polyclonal antibody was immunoreacted against a blot containing the GHM1 immunoprecipitates from the brain lysate a doublet was observed at approximately 100 kDa. When GHM1 was immunoreacted against the same immunoprecipitate the 350 kDa HD protein was also seen The specificity of the HD-HIP1 interaction is seen as no immunoreactive bands seen are as a result of the proteins adsorbing to the Protein-A-Sepharose (Lysate + No Antibody) or when a random, non related antibody (Lysate + anti-Synaptobrevin) is used as the immunoprecipitating antibody.

EXAMPLE 9

Subcellular fractionation of brain tissue

Cortical tissue (20-100 mg/ml) was homogenized, on ice, in a 2 ml pyrex-teflon IKA-RW15 homogenizer (Tekmar Company) in a buffer containing 0.303M sucrose, 20mM Tris-HCl pH 6.9, 1mM $MgCl_2$, 0.5mM EDTA, 1mM PMSF, 1mM leupeptin, soybean trypsin inhibitor and 1mM benzamidine (Wood et al., *Human Molec. Genet.* 5: 481-487 (1996)).

Crude membrane vesicles were isolated by two cycles of a three-step differential centrifugation protocol in a Beckman TLA 120.2 rotor at 4 C based on the methods of Wood et al (1996). The first step precipitated cellular debris and nuclei from tissue homogenates for 5 minutes at 1300 x g (P1). The 1300 x g supernatant was subsequently centrifuged for 20 minutes at 14 000 x g to isolate synaptosomes and mitochondria (P2). Finally, microsomal

and plasma membrane vesicles were collected by a 35 minute centrifugation at 142 000 x g (P3). The remaining supernatant was defined as the cytosolic fraction.

High salt extraction of membranes

Aliquots of P3 membranes were twice suspended at 2mg/ ml in 0.5M NaCl, 10mM Tris-HCl, 2mM $MgCl_2$, pH7.2, containing protease inhibitors (see above). The same buffer without NaCl was used as a control. The membrane suspensions were incubated on ice for 30 minutes and then centrifuged at 142 000 x g for 30 minutes.

Extraction of cytoskeletal and cytoskeletal-associated proteins.

To extract cytoskeletal proteins, crude membrane vesicles from the P3 fraction membrane were suspended in a volume of Triton X-100 extraction buffer to give a protein: detergent ratio of 5:1. The composition of the Triton X-100 extraction buffer was based on the methods of Arai et al., *J. Neuroscience* 38: 348-357 (1994) and contained 2% Triton X-100, 10mM Tris-HCl, 2mM $MgCl_2$, 1mM leupeptin, soybean trypsin inhibitor, PMSF and benzamidine. Membrane pellets were suspended by hand with a round-bottom teflon pestle, and placed on ice for 40 minutes. Insoluble cytoskeletal matrices were precipitated for 35 minutes at 142 000 x g in a Beckman TLA 120.2 rotor. The supernatant was defined as non-cytoskeletal-associated membrane or membrane--associated protein and was removed. The remaining pellet was extracted with Triton X-100 a second time using the same conditions. We defined the final pellet as cytoskeletal and cytoskeletal-associated protein.

Solubilization of protein and analysis by SDS-PAGE and Western Blotting

Membrane and cytoskeletal protein was solubilized in a minimum volume of 1% SDS, 3M urea, 0.1mM dithiothreitol in TBS buffer and sonicated. Protein concentration was determined using the BioRad DC Protein assay and samples were diluted at least 1 X with 5 X sample buffer (250mM Tris-HCl pH 6.8, 10% SDS, 25% glycerol, 0.02% bromophenol blue and 7% 2-mercaptoethanol) and were loaded on 7.5% SDS-PAGE gels (Bio-Rad Mini-PROTEIN II Cell system) without boiling. Western blotting was performed as described above.

Immunohistochemistry

Brain tissue was obtained from a normal C57BL/6 adult (6 months old) male mouse sacrificed with chloroform then perfusion-fixed with 4% v/v paraformaldehyde/0.01 M phosphate buffer (4% PFA). The brain tissues were removed, immersion fixed in 4% PFA for 1 day, washed in 0.01M phosphate buffered saline, pH 7.2 (PBS) for 2 days, and then equilibrated in 25% w/v sucrose PBS for 1 week. The samples were then snap-frozen in Tissue Tek molds by isopentane cooled in liquid nitrogen. After warming to -20 C, frozen blocks derived from frontal cortex, caudate/putamen, cerebellum and brainstem were cut into 14 mm sections for immunohistochemistry. Following washing in PBS, the tissue sections were blocked using 2.5% v/v normal goat serum for 1 hour at room temperature. Primary antibodies diluted with PBS were applied to sections overnight at 4 C. Optimal dilutions for the polyclonal antibodies BKP1 and HIP1 were 1:50. Using washes of 3 x 5 minutes in PBS at room temperature, sections were sequentially incubated with biotinylated secondary antibody and then an avidin-biotin complex reagent (Vecta Stain ABC Kit, Vector) for 60 minutes each at room temperature. Color was developed using 3-3'-diaminobenzidine tetrahydrocholoride and ammonium nickel sulfate.

For controls, sections were treated as described above except that HIP1 antibody aliquots were preabsorbed with an excess of HIP1 peptide as well as a peptide unrelated to HIP1 prior to incubation with the tissue sections.

In situ hybridization

In situ hybridization was performed as previously described with some modification (Suzuki et al, *BBRC* 219: 708-713 (1996)). The RNA probes were prepared using the plasmid gt149 (Lin, B., et al., *Human Molec. Genet.* 2: 1541-1545 (1994)) or a 558 subclone of HIP1. The anti-sense and sense single-stranded RNA probes were synthesized using T3 and T7 RNA polymerases and the In Vitro Transcription Kit (Clontech) with the addition of [α^{35}S]-CTP (Amersham) to the reaction mixture. Sense RNA probes were used as negative controls. For HIP1 studies normal C57BL/6 mice were used. Huntingtin probes were tested on two different transgenic mouse strains expressing full-length huntingtin, cDNA HD10366 (44CAG) C57BL/6 mice and YAC HD10366(18CAG) FVB/N mice. Frozen brain sections

(10um thick) were placed onto silane-coated slides under RNase-free conditions. The hybridization solution contained 40% w/v formamide, 0.02M Tris-HCl (pH 8.0), 0.005M EDTA, 0.3 M NaCl, 0.01M sodium phosphate (pH 7.0), 1x Denhardt's solution, 10% w/v dextran sulfate (pH 7.0), 0.2% w/v sarcosyl, yeast tRNA (500mg/ml) and salmon sperm DNA (200mg/ml). The radiolabelled RNA probe was added to the hybridization solution to give 1 x 106 cpm/200 ul/ section. Sections were covered with hybridization solution and incubated on formamide paper at 65 C for 18 hours. After hybridization, the slides were washed for 30 minutes sequentially with 2x SSC, 1x SSC and high stringency wash solution (50% formamide, 2x SSC and 0.1M dithiothreitol) at 65 C, followed by treatment with RNAse A (1mg/ml) at 37 C for 30 minutes, then washed again and air-dried. The slides were first exposed on autoradiographic film (b-max, Amersham, UK) for 48 hours and developed for 4 minutes in Kodak D-19 followed by a 5 minute fixation in Fuji-fix. For longer exposures, the slides were dipped in autoradiographic emulsion (50% w/v in distilled water, NR-2, Konica, Japan), air-dried and exposed for 20 days at 4 C then developed as described. Sections were counterstained with methyl green or Giemsa solutions.

EXAMPLE 10

We determined a more precise location of the HIP1 gene on chromosome 7 in the context of a physical and genetic map of chromosome 7, and determined its genomic organization. HIP1 maps by FISH and RH mapping to chromosome band 7q11.23, which contains the chromosomal region commonly deleted in Williams-Beuren syndrome (WS). We used several methods to refine the mapping of HIP1 in this region. PCR screening of a chromosome 7-YAC-library (Scherer et al., *mammalian Genome* 3: 179-181 (1992)) with primers from the 3' UTR of HIP1 resulted in the identification of only a single positive YAC clone (HSC7E512). This YAC clone had previously been shown to map near the Williams syndrome commonly deleted region (Osborne et al., *Genomics* 45: 402-406 (1997)). The HIP1 cDNA was then used to screen a chromosome 7 specific cosmid library from the Lawrence Livermore National Laboratory (LL07NC01), and the RPCI genomic P1 derived artificial chromosome (PAC) library (Pieter de Jong, Rosswell Park, Buffalo, NY). Several PAC and cosmid clones that were already part of pre-assembled contigs in the Williams

syndrome region at 7q11.23 were identified (Fig 5). Restriction enzyme digestion, blot hybridization experiments and PCR screening confirmed that the clones contained the HIP1 gene.

We determined the exon-intron boundaries and intron sizes of HIP1. Primers were designed based on the sequence of the HIP1 transcript and used to sequence directly from the cosmid, PAC clone and long PCR products from PAC or genomic DNA. Whenever a PCR fragment generated was longer than predicted from the cDNA sequence, it was assumed to contain an intron. The size of the introns was determined by sequencing the intron directly or by PCR amplification of the introns from both genomic DNA and the cosmid or PAC clone from the region. Three sets of overlapping cosmids and a PAC clone that contain the entire coding sequence of HIP1 were characterized (Fig 5). Cosmid 181G10 and 250F2 were digested with EcoRI and cloned into the plasmid bluescript. Further sequences were generated from these plasmid subclones. Intron-exon boundary sequences were then identified by comparing HIP1 genomic and transcript sequence. The gene is contained within 75 kb and comprises 29 exons and 28 introns. The intron-exon boundary sequences are shown in Table 4, along with the exon and intron sizes. A graphic summary of these data is also shown in Fig. 5. Exons 1 to 28 contained the coding regions. The last and largest exon of the HIP1 gene was found to contain approximately 7 kb. Most of the intron-exon junctions followed the canonical GT-AG rule. An AT was found at the 3' splice site of exon 1 and an AC at the 5' splice site of exon 2. Sequence data from all the exon-intron borders of the coding region and 3'-UTR is set forth in Seq. ID Nos. 16-44. (These sequence have been deposited with GenBank as Accession Nos. AF052261 to AF052288).

Sequence analysis of previously published 5' untranslated region (GenBank accession U79734) revealed the possibility that the open reading frame extends upstream of the ATG in the exon 4 to a 5' ATG in exon 1. Although we failed to obtain any additional 5' sequences despite repeated 5' RACE analyses, an additional ATG, 284 bp upstream of the previously published exon 1 is in the same reading frame and has the surrounding sequence of TGCCATGTT which is similar to the AGCCATGGG, the consensus Kozak sequence (Kozak, M. *Nucl. Acids Res.* 15: 8125-8148 (1987)). If translated from this ATG, the protein would be highly homologous to the N-terminal portion of ZK370.3 and yeast Sla2 protein

(Fig. 6). The translated protein in the region of exons 1 to 3 shows an identity of >40% and similarity of >60% to the N-terminal part of ZK370.3. This suggests that the exons 1 to 3 are probably translated.

In western blot studies, HIP1 is identified as a 120 kd protein (11, 23), while the putative translation of the previously published cDNA gives a protein product of estimated molecular weight of approximately 100 kd. If HIP1 gene were translated from the ATG 284 bp upstream of the exon 1, the expected product would have an estimated molecular weight of 122 kd. RNA PCR studies with primers downstream of this ATG and primers in exon 7 amplify expected products of 576 and 600 bp. Taken together these data support the contention that exon 1 extends further 5' and that HIP1 gene is translated from the ATG in exon 1. Sequence analyses showed no TATA, CAAT box or any GC rich promoter sequence upstream of exon 1 ATG. The promoter prediction programs provided by the server http://dot.imgen.bcm.tmc.edu: 9331/seq.search/gene.search.html did not predict any promoter upstream of the ATG at position -284, (position 0 corresponds to the first nucleotide of published cDNA, GenBank accession U79734). This suggests that HIP1 may have additional exons.

Finally, we evaluated HIP1 gene as a candidate gene for Huntington disease in families without CAG expansion. In a large study of 1022 patients with a clinical diagnosis of HD, no CAG repeat expansion was found in 12 patients who might represent phenocopies of HD. In at least three families, linkage studies have excluded the HD locus at 4p. Mutation in an interacting protein could result in a similar phenotype as illustrated by the discovery of mutations in dystrophin associated proteins in muscular dystrophies. A mutation in HIP1 may result in altered interaction of huntingtin and HIP1 and lead to cellular toxicity as a result of more HIP1 being free in the cytosol. Thus mutations in huntingtin interacting proteins genes may cause a phenotype suggestive of HD. We studied two of the larger families diagnosed with HD without CAG expansion in HD gene, with the highly informative marker D71816 which maps centromeric and very close to HIP1 gene. The clinical findings in both the families were compatible with a diagnosis of HD, although there were atypical features. In family 1733, HIP1 locus appears to be excluded, as there are two recombinants with the marker. Individuals II-5 and II-7 who do not share the haplotype with

the affected individuals are now 41 and 39 years old and have normal neurological examinations.

In the family 1602, a lod score of 1.92 is obtained with the marker D7S1816 at $\theta_{max}=0$. Sequencing of all the coding exons did not reveal any mutation in any exon sequence. The promoter sequence has not been examined. Subsequently a whole genome scan revealed a higher lod scores for markers on chromosome 20p.

EXAMPLE 11

A mouse brain lambda ZAPII cDNA library (Stratagene # 93609) was screened with various mouse ESTs which showed homology to the human HIP1 cDNA sequence (see Fig. 7). The ESTs were initially isolated from the non-redundant Database of GenBank EST Division by performing a BLASTN using a fragment of the human HIP1 cDNA as the query. We obtained 4 different ESTs which showed homology to HIP1: 1) aa110840 (clone 520282) which is 399bp and shows 58% identity, at the nucleotide level, to position 1880 to 2259 of the HIP1 cDNA. 2) w82687 (clone 404331) which is 420bp and shows 66% identity, at the nucleotide level, to position 2750 to 2915 of the HIP1 cDNA. 3) aa138903 (clone 586510) which is 509bp and shows 88% identity, at the nucleotide level, to position 2763 to 2832 of the HIP1 cDNA. 4) aa388714 (569088) which is 404bp and shows 88% identity, at the nucleotide level, to position 2475 to 2692 of the HIP1 cDNA.

mHIP1:

Fifty nanograms of a 362bp KpnI & PvuII fragment of clone 569088 (containing EST aa388714) was radioactively labeled with [32-P]-dCTP using random-priming. The probe was allowed to hybridize to filters containing > 2x 10^5 pfu/ml of the mouse brain lambda ZAPII cDNA library (Stratagene # 93609) overnight at 65°C in Church buffer (0.5M sodium phosphate buffer (pH 7.2), 2.7% SDS, 1mM EDTA). The filters were washed at room temperature for 15 minutes with 2XSSPE, 0.1% SDS, then at 65°C for 20 minutes with 1XSSPE, 0.1%SDS and finally twice at 65°C with 0.5 XSSPE, 0.1%SDS. The filters were exposed to X-ray film (Kodak, XAR5) overnight at -70 C. Primary positives were isolated, replated and subsequent secondary positives were hybridized and washed as for the primary

screen. The resulting positive phage was converted into plasmid DNA by conventional methods (Stratagene) and the cDNA termed 4n-n1, was isolated and sequenced 551bp and 541bp from the T7 and T3 end, respectively. 4n-n1 is 2.2kb in length and the T7 end showed 72% identity, at the nucleotide level, to position 1486 to 1715 of the HIP1 cDNA. The 2.2kb insert from 4n-n1 was excised using EcoR1. Fifty nanograms of the 2.2kb insert was used to produced a radioactive probe and used to screen the mouse brain lambda ZAPII cDNA library (Stratagene # 93609) in the same manner as above. The resulting positive phage was converted into plasmid DNA by conventional methods (Stratagene) and the cDNA termed mHIP1a, was isolated and completely sequenced. mHIP1 is 2.3kb in length and showed 85% identity, at the nucleotide level, to position 726 to 3072 of the HIP1 cDNA.

mHIP1a:

Fifty nanograms of a 1.3kb EcoRI & NcoI fragment of clone 404331 (containing EST w82687) was radioactively labeled with [32-P]-dCTP using random--priming. The probe was allowed to hybridize to filters containing > 2x 10^5 pfu/ml of the mouse brain lambda ZAPII cDNA library (Stratagene # 93609) overnight at 65°C in Church buffer (see above). The filters were washed at room temperature for 15 minutes with 2XSSPE, 0.1% SDS, then at 65°C for 20 minutes with 1XSSPE, 0.1%SDS and finally twice at 65°C with 0.2XSSPE, 0.1%SDS. The filters were exposed to X-ray film (Kodak, XAR5) overnight at -70°C. Primary positives were isolated, replated and subsequent secondary positives were hybridized and washed as for the primary screen. The resulting positive phage was converted into plasmid DNA by conventional methods (Stratagene) and the cDNA termed mHIP1a, was isolated and completely sequenced. mHIP1a is 3.96 kb in length and shows 60% identity, at the nucleotide level, to position 12 to 2703 of the HIP1 cDNA.

EXAMPLE 12

HIP1a:

The entire mHIP1a cDNA sequence was used to screen the non-redundant Database of GenBank EST Division. We identified a human EST, T08283, which showed homology to

mHIP1a. T08383 (clone HIBBB80) is 391bp and shows 87% identity, at the nucleotide level, to position 2904 to 3113 of the mHIP1a cDNA.

Fifty nanograms of a 1.6kb HindIIII & Not1I fragment of clone 404331 (containing EST T08283) was radioactively labeled with [32-P]-dCTP using random-priming. The probe was allowed to hybridize to filters containing > 2x 105 pfu/ml of a human frontal cortex lambda cDNA library overnight at 65 C in Church buffer (see above). The filters were washed at 65 C for 10 minutes with 1XSSPE, O.1% SDS, and then for 30 minutes and 15 minutes with 0.1XSSPE, 0.1%SDS. The filters were exposed to X-ray film (Kodak, XAR5) overnight at -70 C. Primary positives were isolated, replated and subsequent secondary positives were hybridized and washed as for the primary screen. The resulting positive phage was converted into plasmid DNA by conventional methods (Stratagene) and the cDNA termed HIP1a, was isolated and completely sequenced. HIP1a is 3.2 kb in length and shows 53% identity, at the nucleotide level, to position 876 to 3058 of the HIP1 cDNA.

EXAMPLE 13

Following the identification of a 1.2 kb partial human HIP-1 cDNA by yeast two-hybrid interaction studies, a 3.9 kb HIP-1 fragment was isolated from a cDNA library, ligated to a 5' RACE product then subcloned into the mammalian expression vector pCI-neo (Promega). This construct, CMV-HIP-1, expresses HIP-1 from the CMV promoter and was used in the cell expression studies described below. Mouse HIP-1a (mHIP-1a) was also subcloned into a CMV driven expression vector for cell culture expression studies.

EXAMPLE 14

Huntingtin proteins with expanded polyglutamine tracts can aggregate into large, irregularly shaped deposits in HD brains, transgenic mice and in vitro cell culture. We have shown that in HEK (human embryonic kidney) 293T cells the aggregation of full-length and larger huntingtin fragments occurs after the cells have been exposed to a period of apoptotic stress. In order to assess the consequence of HIP-1 expression in cultured cells, we used huntingtin aggregation as one marker of viability.

Human embryonic kidney cells (HEK 293T) were grown on glass coverslips in Dulbecco's modified Eagle medium (DMEM, Gibco, NY) with 10% fetal bovine serum and antibiotics, in 5% CO2 at 37°C. The cells were transfected at 30% confluency with the calcium phosphate protocol by mixing Qiagen-prepared DNA (Qiagen, CA) with 2.5 M $CaCl_2$, then incubating at room temperature for 10 min. 2X HEPES buffer (240 mM NaCl, 3.0 mM Na_2HPO_4, 100 mM HEPES, pH 7.05) was added to the DNA/calcium mixture, incubated at 37°C for 60 sec, then added to the cells. After 12-18 h, the media was removed, the cells were washed and fresh media was added. At 36 h post-transfection, the cells were exposed to an apoptotic stress by treatment with 35 uM tamoxifen (Sigma) for 1 hour, or left untreated, then processed for immunofluorescence. The cells were washed with PBS, fixed in 4% paraformaldehyde/PBS solution for 20 minutes at room temperature then permeabilized in 0.5% Triton X-100/PBS for 5 min. Following three PBS washes, the cells were incubated with anti-huntingtin antibody MAB2166 (Chemicon) (1:2500 dilution) and anti-HIP-1 antibody HIP-1fp (1:100 dilution) in 0.4% BSA/PBS for 1 h at room temperature in a humidified container. The primary antibody was removed, the cells were washed and secondary antibodies conjugated to Texas red or FITC were added at a 1:600-1:800 dilution for 30 min at room temperature. The cells were then washed again, and the coverslips were mounted onto slides with DAPI (4',6'-diamindino-2 phenylindole, Sigma) as a nuclear counter-stain. Immunofluorescence was viewed using a Zeiss (Axioscope) microscope, digitally captured with a CCD camera (Princeton Instrument Inc.) and the images were colourized and overlapped using the Eclipse (Empix Imaging Inc.) software program. Appropriate control experiments were performed to determine the specificity of the antibodies, including secondary antibody only and mock transfected cells.

The huntingtin fragment HD1955 was used in the aggregation studies. This fragment represents the N-terminal 548 amino acids of huntingtin, and corresponds approximately to the polyglutamine-containing fragment produced by caspase 3 cleavage of huntingtin. Transfection of HD1955 with 15 polyglutamines (HD1955-15) results in a diffuse cytoplasmic distribution of the expressed protein. Transfection of HD1955 with 128 polyglutamines (HD1955-128) also results in diffuse cytoplasmic expression. However, exposure of cells transfected with HD1955-128 to tamoxifen results in a marked

redistribution of huntingtin. In 29% of cells expressing HD1955-128, the huntingtin protein appears as dense aggregates that are localized in the perinuclear area of the cell. In contrast, less than 1% of HD1955-128 expressing cells contain aggregates in the absence of tamoxifen, and 0% of HD1955-15 cells form aggregates in the presence or absence of tamoxifen treatment.

Co-transfection of HIP-1 and HD1955 was used to test the influence of HIP-1 on huntingtin aggregation. As a control, b-galactosidase was co-transfected with HD1955. In the control transfections, 1-2% of cells expressing HD1955-128 formed aggregates in the absence of tamoxifen, similar to HD1955-128 expressed alone. However, when HD1955-128 was co-expressed with HIP-1, an average of 14% of huntingtin-expressing cells contained aggregates with no tamoxifen treatment. Double-labeling demonstrated that the majority of the cells containing aggregates also expressed HIP-1, directly implicating HIP-1 in the increase in aggregation. Therefore, these results indicate that HIP-1 provides sufficient stress on the huntingtin-expressing cells to form aggregates, to the extent that tamoxifen is no longer necessary.

EXAMPLE 15

We next designed a series of experiments to identify a region of HIP-1 sufficient for inducing aggregate formation of HD1955-128. As described above, HIP-1 contains a domain with high homology to the death effector domains (DED) present in many apoptosis-related proteins. The DED domain of HIP-1 was ligated in-frame to HD1955-128, 3' from the caspase-3 cleavage site. Transfection of the resulting fusion protein with the DED ligated in the sense orientation (HD1955-128-DEDsense) resulted in a large number (30-50%) of cells containing aggregates, without tamoxifen incubation. In contrast, expression of a huntingtin-DED fusion protein with DED in the antisense orientation (HD1955-128-DEDantisense) did not have more aggregates than the HD1955-128 no tamoxifen control. Therefore, the DED domain of HIP-1 is sufficient to stress the cells, causing aggregate formation.

EXAMPLE 16

To directly assess the effect of HIP-1 expression on cell viability, mitochondrial function tests were performed on 293T cells transfected with HIP-1. The assessment of mitochondrial function, using the MTT assay (Carmichael et al., *Cancer Res.* 47: 936-942 (1987); Vistica et al., *Cancer Res.* 51: 2515-2520 (1991)), is a standard method to measure cell viability. The MTT assay quantitates the formation of a coloured substrate (formazan), with the mitochondria of viable cells forming more substrate than non-viable cells. Since decreased mitochondrial activity is an early consequence of many cellular toxins, the MTT assay provides an early indicator of cell damage.

For cell viability assays, HEK 293T cells were seeded at a density of 5×10^4 cells into 96-well plates and transfected with 0.1 ug or 0.08 ug HIP-1 or 0.1 ug of the control construct lacZ using the calcium phosphate method described above. At 24-36 hours post-transfection tamoxifen-treated cells were incubated for 2 hours in a 1:10 dilution of WST-1 reagent (Boehringer Mannheim) and release of formazan from mitochondria was quantified at 450 nm using an ELISA plate reader (Dynatech Laboratories) (Carmichael et al., 1987; Mosmann, *J. Immunol. Meth* 65: 55-63 (1983)). One way ANOVA and Newman-Keuls test were used for statistical analysis. The transfection efficiency, measured by β-galactosidase staining and immunofluoresence, was approximately 50%.

We have previously demonstrated that expression of mutant huntingtin results in increased susceptibility to an apoptotic stress induced by sub-lethal doses of tamoxifen in transfected 293T cells (Martindale et al., 1998). A similar assay was used to test the consequence of HIP-1 expression. With 0.1 ug transfected HIP-1 DNA, after 24 hr expression, HIP-1 resulted in increased cell death in response to tamoxifen, compared with the tamoxifen-treated β-galactosidase control ($p<0.01$, $n=4$). Reducing the amount of transfected HIP-1 DNA to 0.08 ug also resulted in increased cell death compared with control ($p<0.01$, $n=4$), indicating the high potency of HIP-1 (Fig. 8). Furthermore, increased cell death in cells transfected with HIP-1 was observed in the absence of apoptotic stress at 48 hrs post-transfection, but was so severe that is could not be accurately quantitated. Thus, an earlier time point (24 hr) had to be used for better reproducibility, using an apoptotic stress to unmask the phenotype.

In order to model a pathogenic interaction of HIP-1 and huntingtin in the HEK 293 mammalian cell system, HIP-1 was transfected into cell lines stably expressing huntingtin. Two cell lines were chosen for the initial studies, one line expressed the truncated HD1955 construct with 15 glutamines, and the second expressed the HD1955 with 128 repeats. Western blotting indicated that the cell lines expressed huntingtin at similar levels. To assess whether HIP-1 is toxic in the presence of mutant huntingtin, 0.1 ug HIP-1 DNA was transfected into the HD1955-128 cell line. Transfection of HIP-1 into the HD1955-15 cell line was used as the wild-type huntingtin control, and transfection of LacZ into both cell lines was the control for transfection-related toxicity (Figs 9A and 9B). MTT toxicity assays showed that HIP-1 in the presence of mutant huntingtin (HD1955-128) was significantly more toxic than HIP-1 with wild-type huntingtin (HD1955-15), $p<0.001$, $n=4$ (Fig. 9C). This toxicity was observed at 24 hr and 36 hr post-transfection. No tamoxifen was needed to unmask the phenotype, suggesting that the combined cell stress of HIP-1 with truncated huntingtin was sufficient to reduce cell viability over control.

CLAIMS

1. A polypeptide comprising the sequence given by Seq. ID. No. 5.

2. A cDNA molecule comprising the sequence given by Seq. ID No. 6.

3. A polypeptide comprising the sequence given by Seq. ID No. 7.

4. A method for ameliorating the effects of Huntington's disease in a patient expressing a HIP-apoptosis modulating protein, comprising the step of administering the patient a therapeutic composition which reduces the activity of the HIP-apoptosis modulating protein.

5. A method according to claim 4, wherein the composition comprises a material which binds to HIP-apoptosis modulating protein.

6. The method according to claim 4, wherein the composition comprises an expression vector encoding huntingtin having a normal number of repeats.

7. An expression vector for expression of a gene in a mammalian host comprising a region encoding an HD-interacting polypeptide.

8. The expression vector according to claim 7, wherein the HD-interacting polypeptide is an HIP-apoptosis modulating protein.

9. The expression vector according to claim 8, wherein the HIP-apoptosis modulating protein has a sequence which includes the amino acid sequences given by SEQ ID Nos. 2, 4, 5 or 7.

10. The expression vector of claim 7, wherein the HD-interacting polypeptide interacts differently with expanded Huntingtin than with Huntingtin having a CAG repeat region containing 15 to 35 repeats.

11. The expression vector according to claims of claims 7-10, further comprising a region encoding Huntingtin having a polyglutamine tract of 35 or fewer.

12. A method for inducing apoptotic death in cells, comprising the step of introducing into the cells an expression vector encoding at least the death effector domain of a HIP-apoptosis modulating protein whereby the death effector domain is expressed by the cells.

13. The method of claim 12, wherein the expression vector encodes the amino acid sequence given by Seq. ID. No. 2.

14. The method of claim 12, wherein the expression vector encodes the amino acid sequence given by Seq. ID. No. 4.

15. A method for screening a composition for the ability to inhibit apoptosis induced by an HIP-apoptosis modulating protein, comprising simultaneously exposing a population of cells to the composition and an HIP-apoptosis modulating protein and measuring the extent of cell death.

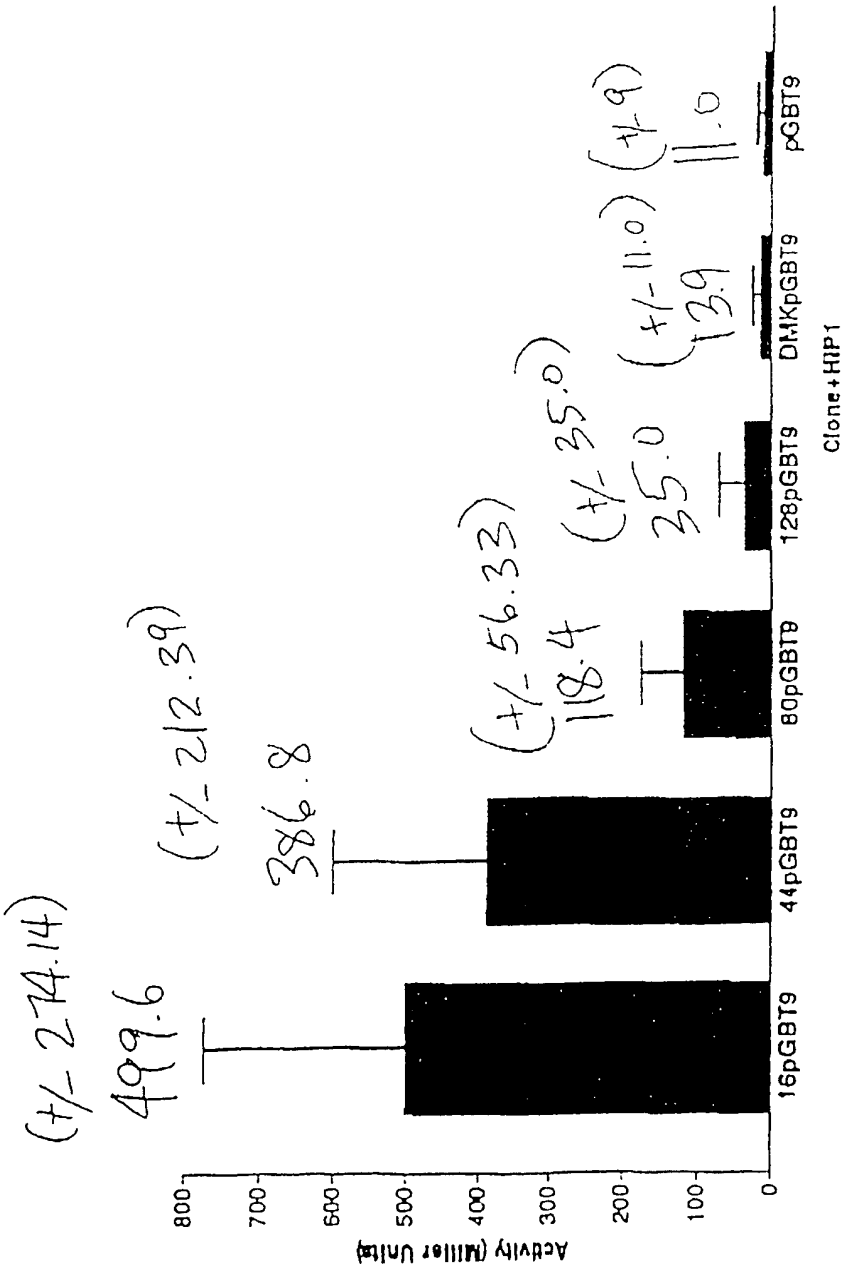

Activity (Miller Units)
800
700
600
500
400
300
200
100
0
16pGBT9
44pGBT9
80pGBT9
128pGBT9
DMKpGBT9
pGBT9
Clone+HIP1
(+/- 274.14)
499.6
(+/- 212.39)
386.8
(+/- 56.33)
118.4
(+/- 35.0)
35.0
(+/- 11.0)
13.9
(+/-9)
11.0

Fig. 1

Fig 2

HIP1 Clones: Nucleotide Alignment

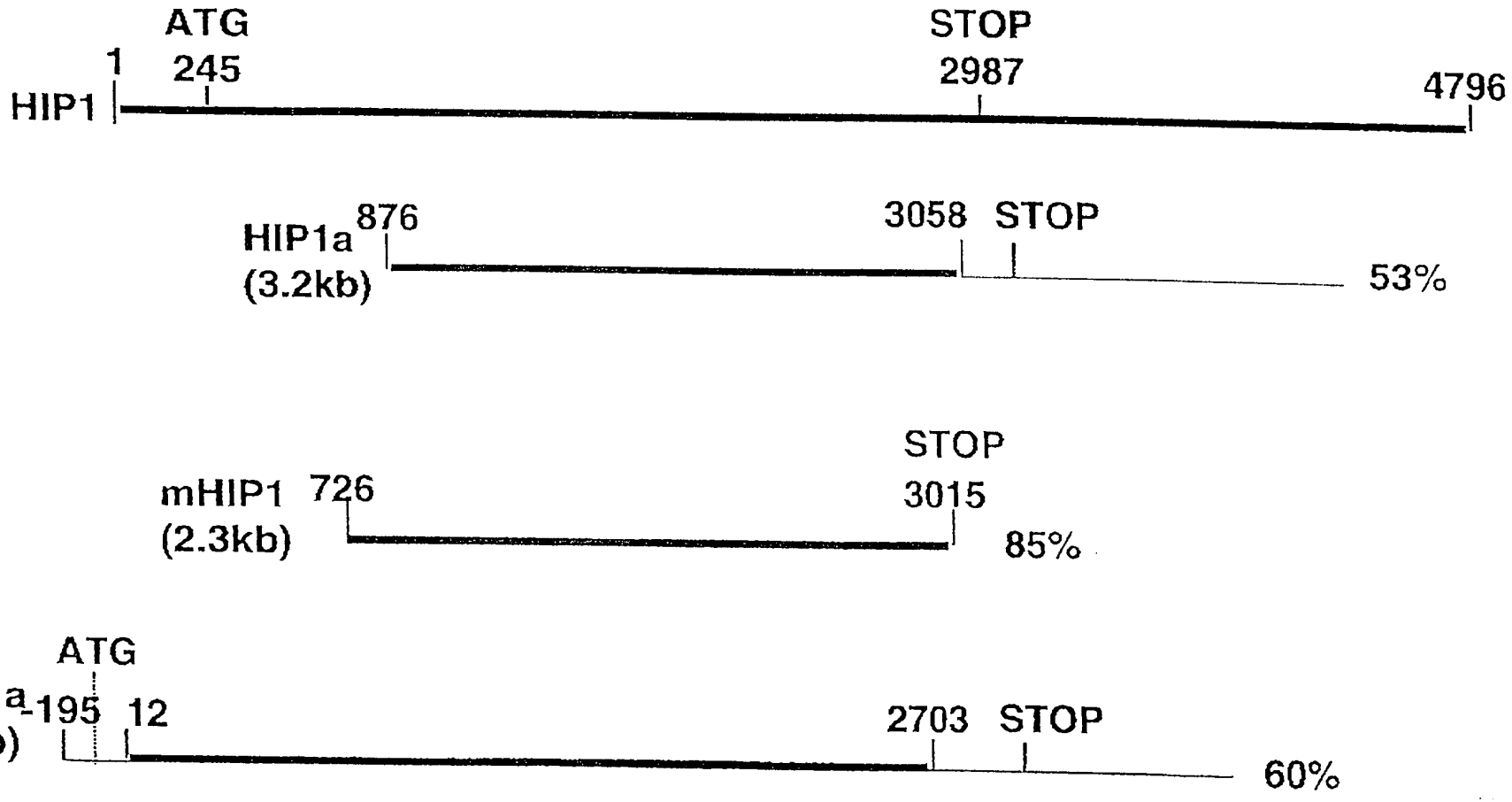


Fig 3

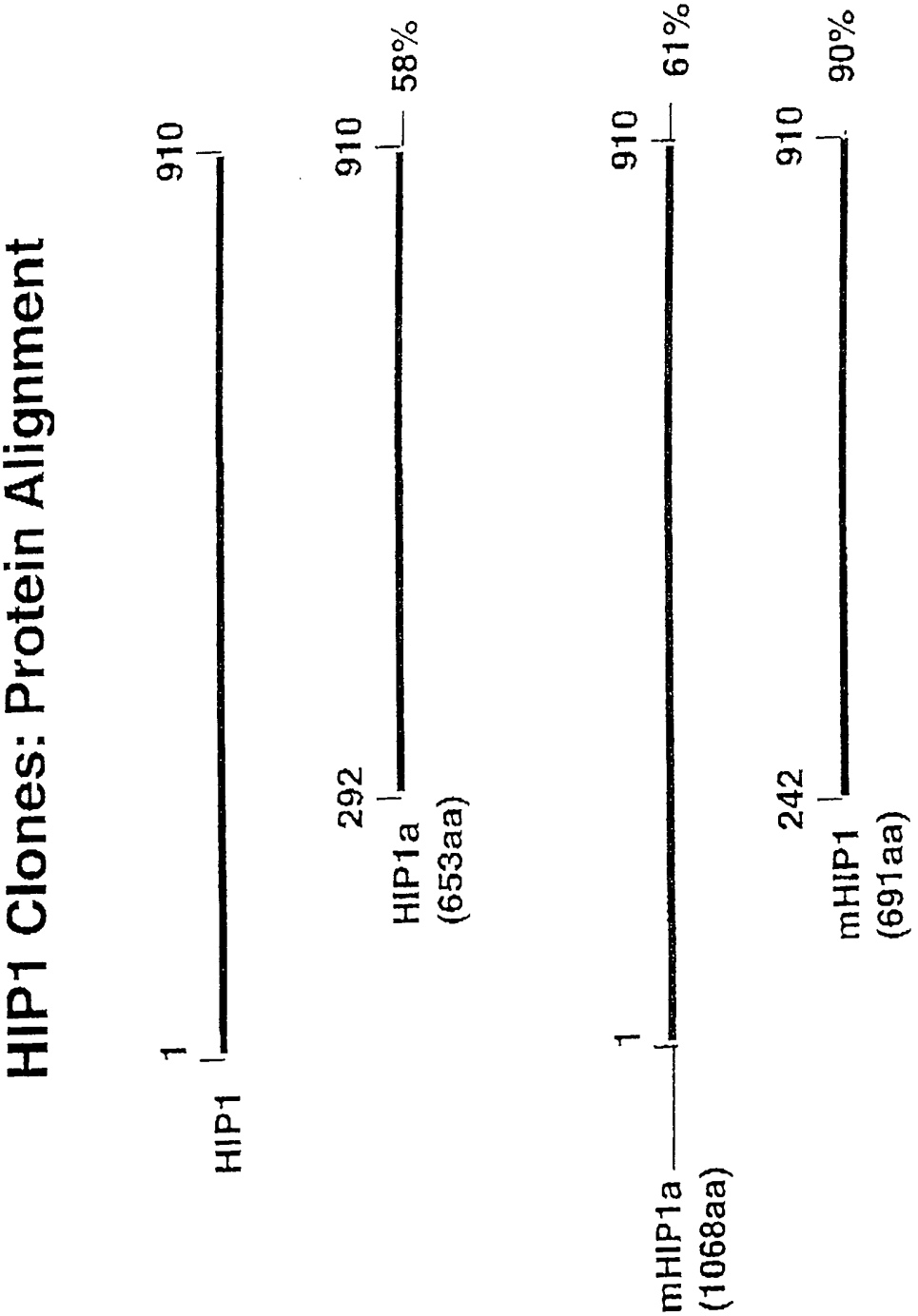

HIP1 Clones: Protein Alignment
1
910
HIP1
292
910
58%
HIP1a
(653aa)
1
910
61%
mHIP1a
(1068aa)
242
910
90%
mHIP1
(691aa)

Fig 4

>Usurpin A
SAEVIHQVEEALDTDEKKMLLFLCRDVAIDVVPPNVRDLLDILRERGKLSVCDLAELLYRVHRFDLLKRILK

>Usurpin B
YRVLMAHIGEDLDKSDVSSLIFLMKDYMGRGKISKHKSFLDLVVELHKLNLVAPDQLDLLEKCLKNIHRIDLKTKIQK

>Casp-8 A
FSRNLYDIGELQDSEDLASLKELSLDYIPQRKQEPIKDALMIFQRLQEKRMLEESNLSFLKELLFRINRLDLLITYLN

>Casp-8 B
YRVMLYQISEEVSREELRSFKFLLQHEISKCKLDDDMNLLDIFIEMEKRVILGEGKLDILKRVCAQINKSLLKIND

>Casp-10 A
FRHKLLTIDSNLGVQDVENLKFLCIGLVPNKKLEKSSSASDVFEHLLAHDLLSEEDPFFLAELLYIIRQKKLLQHLNC

>Casp-10 B
FRNLLYELSEGIDSENLKDMIFLLKDSLPKTEMTSLSFLAFLEKQGKIDEDNLTCLEDLCKTVVPKLLRNIEK

>FADD
FLVLLHSVSSSLSSSELTELKFLCLGRVGKRKLERVQSGLDLFSMLLEQNDLEPGHTELLRELLASLRRHDLLRRVDD

>MC159 A
SLPFLRHLLEELDSHEDSLLLFLGHDAAPGCTTVTQALCSLSQQRKLTLAALVEMLYVLQRMDLLKSRFG

>MC159 B
YHKLMVCVGEELDSSELRALRLFACNLNPSLSTALSESSRPVELVLALENVGLVSPSSVSVLADMLRTLRRLDLCQQLVE

>E8
FRCLMALVNDFLSDKEVEEHYFLCAPRLESHLEPGSKKSFLRLASLLEDLELLGGDKLTFLRHLLTTIGRADLVKNLQV

>KS orfk13A
TYEVLCEVARKLGTDDREVVLFLLNVFLPQPTLAQLIGALRALKEEGRLTFPLLAECLPRAGRRDLLRDLLH

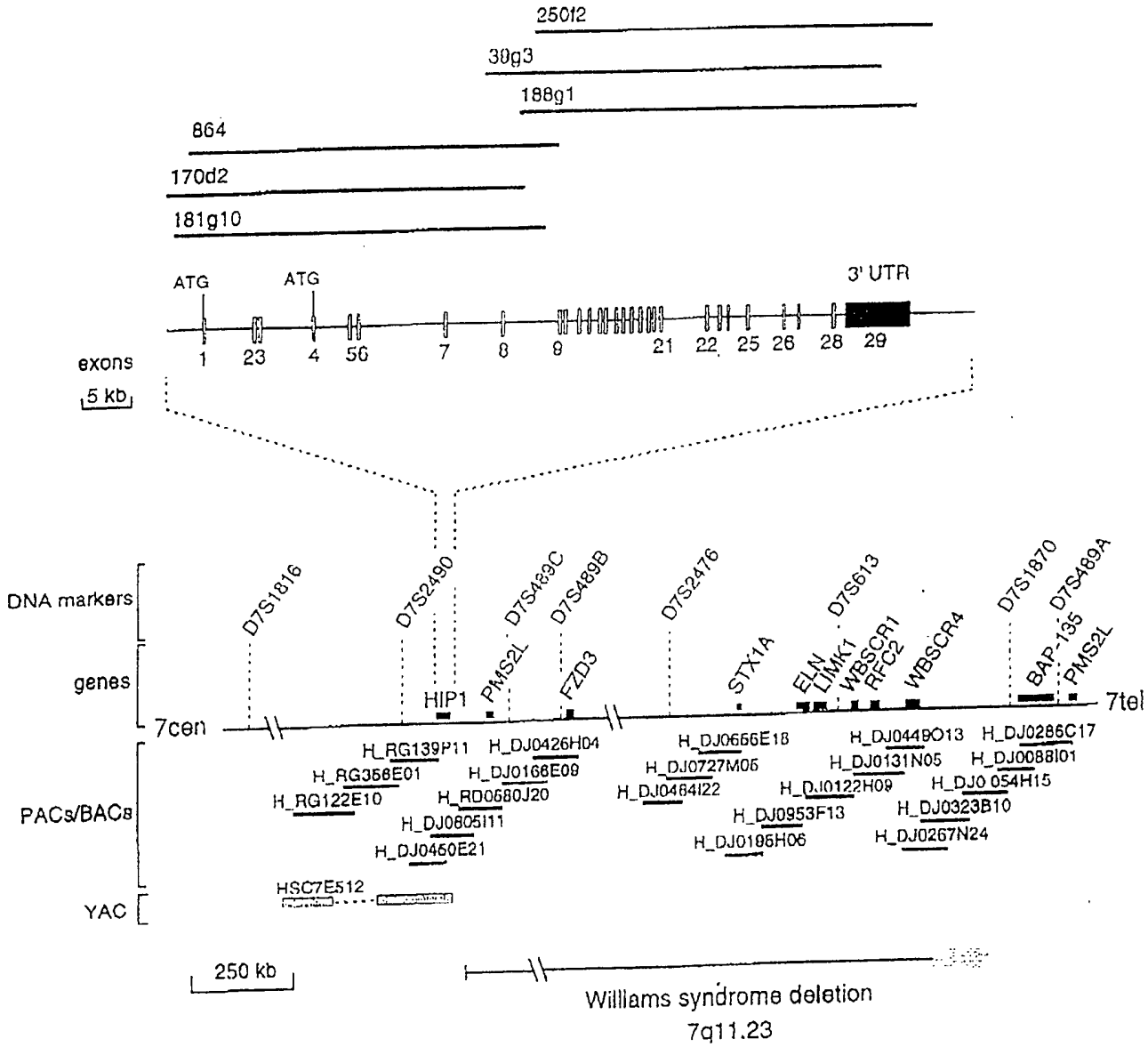
>KS orfk13B
YQLTVLHVDGELCARDIRSLIFLSKDTIGSRSTPQTFLHNVYCMENLDLLGPTDVDALMSMLRSLSRVDLQRQVQT

>HIP1
SELEADLAEQQHLRQQAADDCEFLRAELDELRRQREDTEKAQRSLSEIERKAQANEQRYSKLKEKYSELVQNHADLLRKN
AE

>HIP1a
GELEEQRKQKQKALVDNEQLRHELAQLRAAQLERERSQGLREEAERKASATEARYNKLKEKHSELVHVHAELLRKNAD

>mHIP1a
NGLEAELEEQRKQKQKALVDNEQLRHELAQLKALQLEGARNQGLREEAERKASATEARYSKLKEKHSELINTHAELLRKN
AD

>mHIP1
SELEAELAEQQHLGRQAMDDCEFLRTELDELKRQREDTEKAQRSLTEIERKAQANEQRYSKLKEKYSELVQNHADLLRKN
AE


250f2
30g3
188g1
864
170d2
181g10
ATG
ATG
3' UTR
exons
1 23 4 56 7 8 9 21 22 25 26 28 29
5 kb
DNA markers
genes
PACs/BACs
YAC
D7S1816
D7S2490
D7S489C
D7S489B
D7S2476
D7S613
D7S1870
D7S489A
HIP1
PMS2L
FZD3
STX1A
ELN
LIMK1
WBSCR1
RFC2
WBSCR4
BAP-135
PMS2L
7cen
7tel
H_RG139P11
H_DJ0426H04
H_RG356E01
H_DJ0168E09
H_RG122E10
H_RD0680J20
H_DJ0805I11
H_DJ0460E21
HSC7E512
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H_DJ0727M06
H_DJ0464I22
H_DJ0953F13
H_DJ0195H06
H_DJ0449O13
H_DJ0131N05
H_DJ0122H09
H_DJ0286C17
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250 kb
Williams syndrome deletion
7q11.23

Fig 5

Fig 6

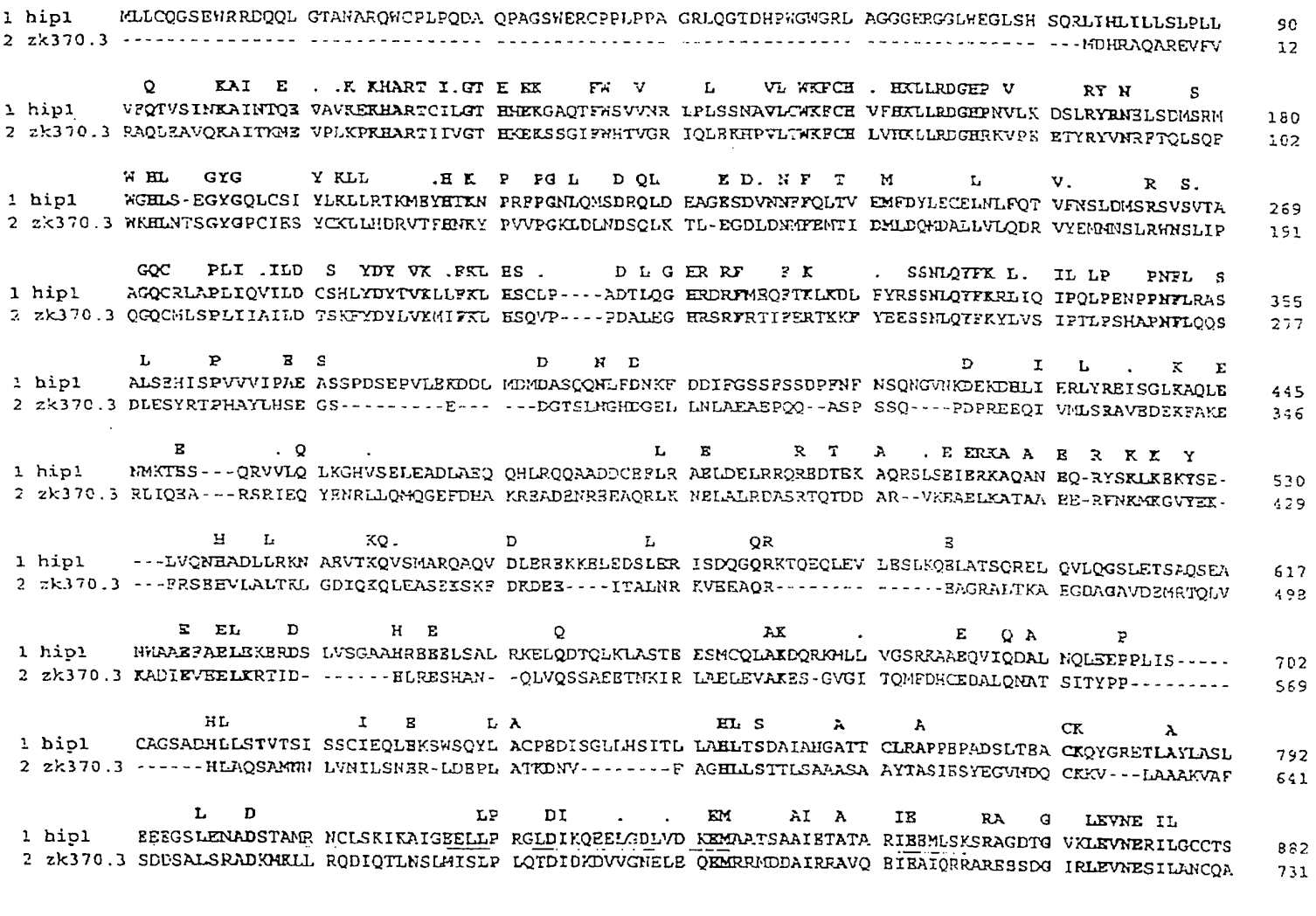

1 hip1 MLLCQGSEWRRDQQL GTANARQWCPLPQDA QPAGSWERCPPLPPA GRLQGTDHPWGWGRL AGGGERGGLWEGLSH SQRLTHLILLSLPLL 90
2 zk370.3 --- MDHRAQAREVFV 12
1 hip1 VPQTVSINKAINTQE VAVREKHARTCILGT HHEKGAQTFWSVVNR LPLSSNAVLCWKFCH VFHKLLRDGHPNVLK DSLRYRNELSDMSRM 180
2 zk370.3 RAQLEAVQKAITKNE VPLKPKHARTIIVGT HKEKSSGIFWHTVGR IQLRKHPVLTWKFCH LVHKLLRDGHRKVPS ETYRYVNRFTQLSQF 102
1 hip1 WGHLS-EGYGQLCSI YLKLLRTKMEYHTKN PRPPGNLQMSDRQLD EAGESDVNNFFQLTV EMFDYLECELNLFQT VFNSLDMSRSVSVTA 269
2 zk370.3 WKHLNTSGYGPCIES YCKLLHDRVTFENKY PVVPGKLDLNDSQLK TL-EGDLDNMFENTI EMLDQMDALLVLQDR VYEMMNSLRWNSLIP 191
1 hip1 AGQCRLAPLIQVILD CSHLYDYTVKLLFKL ESCLP----ADTLQG ERDRFMRQFTKLKDL FYRSSNLQTFKRLIQ IPQLPENPPNFLRAS 355
2 zk370.3 QGQCMLSPLIIAILD TSKFYDYLVKMIFKL ESQVP----PDALEG HRSRYRTIFERTKKF YEESSNLQTFKYLVS IPTLPSHAPNFLQQS 277
1 hip1 ALSEHISPVVVIPAE ASSPDSEPVLEKDDL MDMDASQQNLFDNKF DDIFGSSFSSDPFNF NSQNGVNKDEKDELI ERLYREISGLKAQLE 445
2 zk370.3 DLESYRTPHAYLHSE GS---------E--- ---DGTSLNGHDGEL LNLAEAEPQQ--ASP SSQ----PDPREEQI VMLSRAVEDEKFAKE 346
1 hip1 NMKTSS---QRVVLQ LKGHVSELEADLAEQ QHLRQQAADDCEFLR AELDELRRQREDTEK AQRSLSEIERKAQAN EQ-RYSKLKEKYSE- 530
2 zk370.3 RLIQEA---RSRIEQ YENRLLQMQGEFDHA KREADENRSEAQRLK NELALRDASRTQTDD AR--VKEAELKATAA EE-RFNKMKGVYEK- 429
1 hip1 ---LVQNEADLLRKN ARVTKQVSMARQAQV DLERKKKELEDSLER ISDQGQRKTQEQLEV LESLKQELATSQREL QVLQGSLETSAQSEA 617
2 zk370.3 ---FRSEEVLALTRL GDIQKQLEASEKSKF DRDEK----ITALNR KVEEAQR-------- ------EAGRALTKA EGDAGAVDEMRTQLV 498
1 hip1 NWAAEFAELEKERDS LVSGAAHRKEELSAL RKELQDTQLKLASTE ESMCQLAKDQRKHLL VGSRRAAEQVIQDAL NQLEEPPLIS----- 702
2 zk370.3 KADIEVEELKRTID- ------ELRESHAN- -QLVQSSAEETNKIR LAELEVAKES-GVGI TQMFDHCEDALQNAT SITYPP--------- 569
1 hip1 CAGSADHLLSTVTSI SSCIEQLEKSWSQYL ACPEDISGLIHSITL LAELTSDAIAHGATT CLRAPPEPADSLTEA CKQYGRETLAYLASL 792
2 zk370.3 ------HLAQSAMTN LVNILSNER-LDEPL ATKDNV--------F AGHLLSTTLSAAASA AYTASIESYEGVNDQ CKKV---LAAAKVAF 641
1 hip1 EEEGSLENADSTAMR NCLSKIKAIGEELLP RGLDIKQEELGDLVD KEMAATSAAIETATA RIEEMLSKSRAGDTG VKLEVNERILGCCTS 882
2 zk370.3 SDESALSRADKMKLL RQDIQTLNSLMISLP LQTDIDKDVVGNELE QKMRRMDDAIRRAVQ EIEAIQRRARESSDG IRLEVNESILANCQA 731

FIG 6 (CONT.)

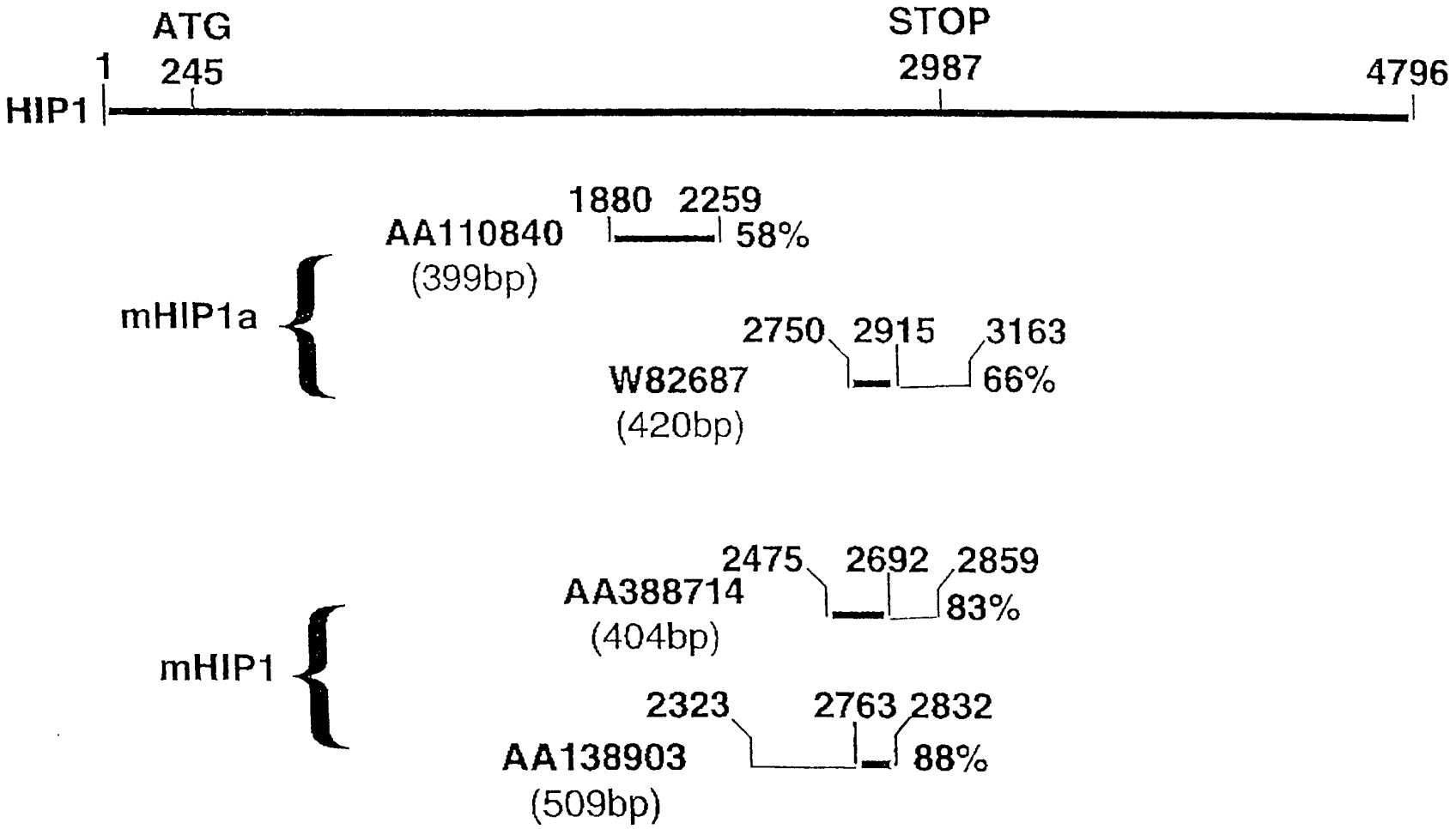
```
          EM .I  L..AS  L Q EIV       SP  KFY  N  MT3GLIS A KAVG  A V V   AD VV GRGK    F E L V   EIAASTA
1 hip1    LMQAIQVLIVASKDL QREIVESGRGTASPK EFYARNSRHTEGLIS ASKAVGWGATVHVDA ADLVVQGRGK----F KELAVCSHEIAASTA    958
2 zk370.3 LMSVIMQLVLASREL QTEIVAAGKAGGSPA EFYKRNHQHTEGLLS AAKAVGVAARVLVES ADGVVTGKGK----F KHLIVAAQEIAASTA    817

          QL . S VKADKDSS  L  L  A   VNQ  TA VVA   G  .        D?S   L    K  EK SQV  L ELE  L  ER KL
1 hip1    QLVAASKVKADKDSP NLAQLQQASRGVNQA TAGVVASTISGKSQI BETDN--MDFSSMTL TQIKRQEMDSQVRVL ELENELQKERQKLGE  1056
2 zk370.3 QLFVSSPVKADKDSS KLDALSVAAKAVNQN TAQVVARVKNGQTTL NDEGS--LDFSYLSL HAAKKEEMESQVKHL ELEQSLNQERAKLAA   905

          LRK HY  A .
1 hip1    LRKKHYELAGVAEGW EEGTEASPPTLQEVV TEKE   1090
2 zk370.3 LRKQHYHMAQLVANK VSP---------- ----    923
```

Fig 7

Mouse ESTs



Hip 1 increases the susceptibility to cell stress.

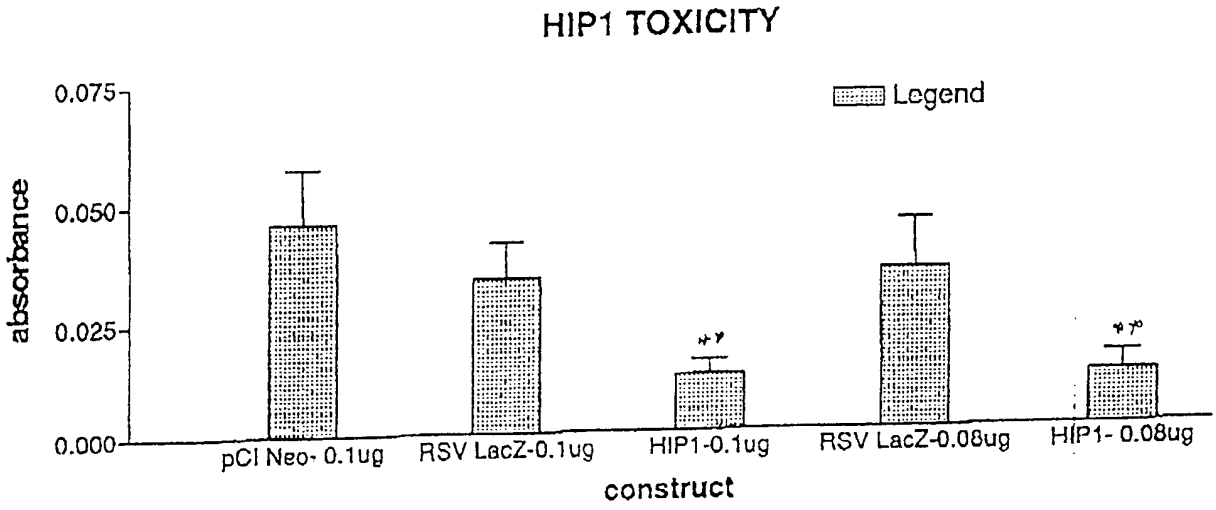


Fig 8

Hip-1 is toxic in the presence of huntingtin

HIP1 transfected into HD1955-15 stable cell line
36 hr post-tansfection

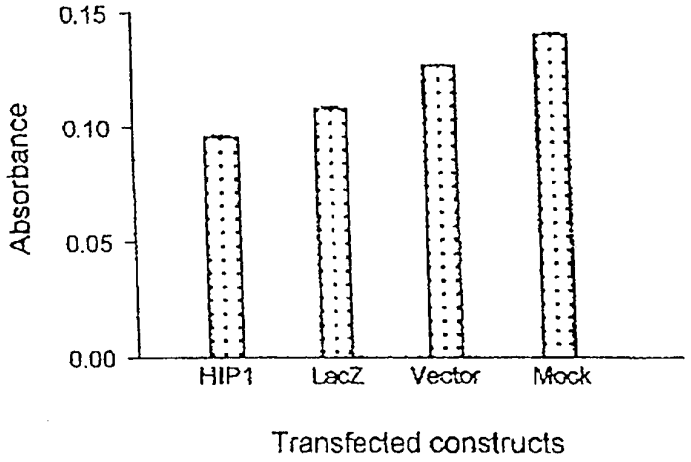


Fig 9A

Hip-1 is toxic in the presence of huntingtin

HIP1 transfected into HD1955-128 stable cell line
36 hr post-tansfection

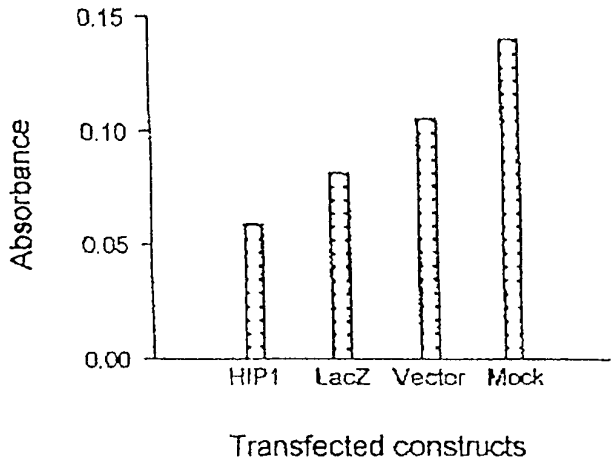


Fig 9B

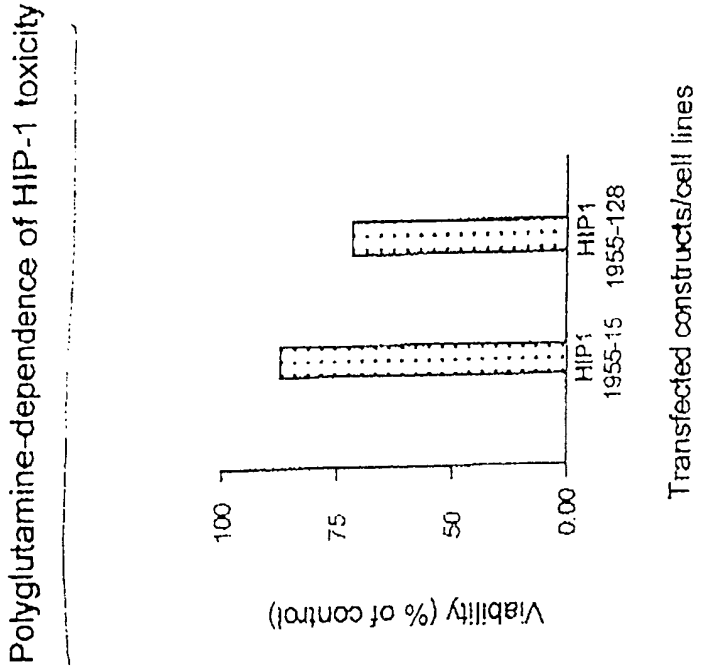

Polyglutamine-dependence of HIP-1 toxicity
Viability (% of control)
100
75
50
0.00
HIP1
1955-15
HIP1
1955-128
Transfected constructs/cell lines

Fig 9C

SEQUENCE LISTING

(1) GENERAL INFORMATION:
(i) APPLICANT:Kalchman, Michael
Hayden. Michael R.
Hackam, Abigail
Chopra, Vikramjit Singh
Nicholson, Donald W.
Vallaincourt, John P.
Rasper, Dita M.
(ii) TITLE OF INVENTION: Apoptosis Modulators That Interact with the Huntington's Disease Gene
(iii) NUMBER OF SEQUENCES: 44
(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Oppedahl & Larson
(B) STREET: PO Box 5270
(C) CITY: Frisco
(D) STATE: CO
(E) COUNTRY: USA
(F) ZIP: 80443-5270
(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette, 3.50 inch, 1.44 Kb storage
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: MS DOS 5.0
(D) SOFTWARE: WordPerfect
(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:
(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Larson, Marina T.
(B) REGISTRATION NUMBER: 32038
(C) REFERENCE/DOCKET NUMBER: UBC.P-013US2
(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (970) 668-2050
(B) TELEFAX: (970) 668-2052

(2) INFORMATION FOR SEQ ID NO:1:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1164
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
(xi)SEQUENCE DESCRIPTION: SEQ ID NO:1:

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ACAGCTGACA CCCTGCAAGG CCACCGGGAC CGCTTCATGG AGCAGTTTAC   50
AAAGTTGAAA GATCTGTTCT ACCGCTCCAG CAACCTGCAG TACTTCAAGC  100
GGGTCATTCA GATCCCCCAG CTGCCTGAGA ACCCACCCAA CTTCCTGCGA  150
GCCTCAGCCC TGTCAGAACA TATCAGCCCT GTGGTGGTGA TCCCTGCAGA  200
GGCCTCATCC CCCGACAGCG AGCCAGTCCT AGAGAAGGAT GACCTCATGG  250
ACATGGATGC CTCTCAGCAG AATTTATTTG ACAACAAGTT TGATGACNTC  300
TTTGGCAGTT CATCCAGCAG TGATCCCTTC AATTTCAACA GTCAAAATGG  350
TGTGAACAAG GATGAGAAGG ACCACTTAAT TGAGCGACTA TACAGAGAGA  400
TCAGTGGATT GAAGGCACAG CTAGAAAACA TGAAGACTGA GAGCCAGCGG  450
GTTGTGCTGC AGCTGAAGGG CCACGTCAGC GAGCTGGAAG CAGATCTGGC  500
CGAGCAGCAG CACCTGCGGC AGCAGGCGGC CGACGACTGT GAATTCCTGC  550
GGGCAGAACT GGACGAGCTC AGGNGGCAGC GGGAGGACAC CGAGAAGGCT  600
CAGCGGAGCC TGTCTGAGAT AGAAAGGAAA GCTCAAGCCA ATGAACAGCG  650
ATATAGCAAG CTAAAGGAGA AGTACAGCGA GCTGGTTCAG AACCACGCTG  700
ACCTGCTGCG GAAGAATGCA GAGGTGACCA AACAGGTGTC CATGGCCAGA  750
CAAGCCCAGG TAGATTTGGA ACGAGAGAAA AAAGAGCTGG AGGATTCGTT  800
GGAGCGCATC AGTGACCAGG GCCAGCGGAA GACTCAAGAA CAGCTGGAAG  850
TTCTAGAGAG CTTGAAGCAG GAACTTGGCA CAAGCCAACG GGAGCTTCAG  900
GTTCTGCAAG GCAGCCTGGA AACTTCTGCC CAGTCAGAAG CAAACTGGGC  950
AGCCGAGTTC GCCGAGCTAG AGAAGGAGCG GGACAGCCTG GTGAGTGGCG 1000
CAGCTCATAG GGAGGAGGAA TTATCTGCTC TTCGGAAAGA ACTGCAGGAC 1050
ACTCAGCTCA AACTGGCCAG CACAGAGGAA TCTATGTGCC AGCTTGCCAA 1100
AGACCAACGA AAAATGCTTC TGGTGGGGTC CAGGAAGGCT GCGGAGCAGG 1150
TGATACAAGA CGCG                                        1164
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(2) INFORMATION FOR SEQ ID NO:2:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 386
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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Thr Ala Asp Thr Leu Gln Gly His Arg Asp Arg Phe Met Glu Gln
 1               5                  10                  15

Phe Thr Lys Leu Lys Asp Leu Phe Tyr Arg Ser Ser Asn Leu Gln
            20                  25                  30

Tyr Phe Lys Arg Val Ile Gln Ile Pro Gln Leu Pro Glu Asn Pro
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35 40 45

Pro Asn Phe Leu Arg Ala Ser Ala Leu Ser Glu His Ile Ser Pro
50 55 60

Val Val Val Ile Pro Ala Glu Ala Ser Ser Pro Asp Ser Glu Pro
65 70 75

Val Leu Glu Lys Asp Asp Leu Met Asp Met Asp Ala Ser Gln Gln
80 85 90

Asn Leu Phe Asp Asn Lys Phe Asp Asp Phe Gly Ser Ser Ser Ser
95 100 105

Ser Asp Pro Phe Asn Phe Asn Ser Gln Asn Gly Val Asn Lys Asp
110 115 120

Glu Lys Asp His Leu Ile Glu Arg Leu Tyr Arg Glu Ile Ser Gly
125 130 135

Leu Lys Ala Gln Leu Glu Asn Met Lys Thr Glu Ser Gln Arg Val
140 145 150

Val Leu Gln Leu Lys Gly His Val Ser Glu Leu Glu Ala Asp Leu
155 160 165

Ala Glu Gln Gln His Leu Arg Gln Gln Ala Ala Asp Asp Cys Glu
170 175 180

Phe Leu Arg Ala Glu Leu Asp Glu Leu Arg Gln Arg Glu Asp Thr
185 190 195

Glu Lys Ala Gln Arg Ser Leu Ser Glu Ile Glu Arg Lys Ala Gln
200 205 210

Ala Asn Glu Gln Arg Tyr Ser Lys Leu Lys Glu Lys Tyr Ser Glu
215 220 225

Leu Val Gln Asn His Ala Asp Leu Leu Arg Lys Asn Ala Glu Val
230 235 240

Thr Lys Gln Val Ser Met Ala Arg Gln Ala Gln Val Asp Leu Glu
245 250 255

Arg Glu Lys Lys Glu Leu Glu Asp Ser Leu Glu Arg Ile Ser Asp
260 265 270

Gln Gly Gln Arg Lys Thr Gln Glu Gln Leu Glu Val Leu Glu Ser
275 280 285

Leu Lys Gln Glu Leu Gly Thr Ser Gln Arg Glu Leu Gln Val Leu

290 295 300

Gln Gly Ser Leu Glu Thr Ser Ala Gln Ser Glu Ala Asn Trp Ala
305 310 315

Ala Glu Phe Ala Glu Leu Glu Lys Glu Arg Asp Ser Leu Val Ser
320 325 330

Gly Ala Ala His Arg Glu Glu Glu Leu Ser Ala Leu Arg Lys Glu
335 340 345

Leu Gln Asp Thr Gln Leu Lys Leu Ala Ser Thr Glu Glu Ser Met
350 355 360

Cys Gln Leu Ala Lys Asp Gln Arg Lys Met Leu Leu Val Gly Ser
365 370 375

Arg Lys Ala Ala Glu Gln Val Ile Gln Asp Ala
380 385 386

(2) INFORMATION FOR SEQ ID NO:3:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4796
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 3:

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CAGTGTACGG TTGATCATAT AACGCCGCGG GCGGGGATTG GTTTATATAT     50
CGCAAATTGA TNTAGGGGGG GGGGGATGGN CAGAGATTTC GCTTCATTAG    100
GCCATTATAA GCAGGAAGGG TTTCAAGGAA AAAAACCCAG AAAGTGCATA    150
TTGCACCCAC CATGAGAAAG GGGCAACAGA CCTTNTGTTN TGTTNTCAAC    200
CGCCTGCTTC TGTTTTAGCA ACGCAGTGTT TTGGTGGAAG TTGTGCCATG    250
TGTTCCACAA ANTCTTCCGA GATGGACACC CGAACGTCCT GAAGGACTTT    300
GTGAGATACA GAAATGAATT GAGTGACATG AGCAGGATGT GGGGCCACCT    350
GAGCGAGGGG TATGGCCAGC TGTGCAGCAT CTACCTGAAA CTGCTAAGAA    400
CCAAGATGGA GTACCACACC AAAAATCCCA GGTTCCCAGG CAACCTGCAG    450
ATGAGTGACC GCCAGCTGGA CGAGGCTGGA GAAAGTGACG TGAACAACTT    500
TTTCCAGTTA ACAGTGGAGA TGTTTGACTA CCTGGAGTGT GAACTCAACC    550
TCTTCCAAAC AGTATTCAAC TCCCTGGACA TGTCCCGCTC TGTGTCCGTG    600
ACGGCAGCAG GGCAGTGCCG CCTCGCCCCG CTGATCCAGG TCATCTTGGA    650
CTGCAGCCAC CTTTATGACT ACACTGTCAA GCTTCTCTTC AAACTCCACT    700
CCTGCCTCCC AGCTGACACC CTGCAAGGCC ACCGGGACCG CTTCATGGAG    750
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CAGTTTACAA AGTTGAAAGA TCTGTTCTAC CGCTCCAGCA ACCTGCAGTA 800
CTTCAAGCGG CTCATTCAGA TCCCCCAGCT GCCTGAGAAC CCACCCAACT 850
TCCTGCGAGC CTCAGCCCTG TCAGAACATA TCAGCCCTGT GGTGGTGATC 900
CCTGCAGAGG CCTCATCCCC CGACAGCGAG CCAGTCCTAG AGAAGGATGA 950
CCTCATGGAC ATGGATGCCT CTCAGCAGAA TTTATTTGAC AACAAGTTTG 1000
ATGACATCTT TGGCAGTTCA TTCAGCAGTG ATCCCTTCAA TTTCAACAGT 1050
CAAAATGGTG TGAACAAGGA TGAGAAGGAC CACTTAATTG AGCGACTATA 1100
CAGAGAGATC AGTGGATTGA AGGCACAGCT AGAAAACATG AAGACTGAGA 1150
GCCAGCGGGT TGTGCTGCAG CTGAAGGGCC ACGTCAGCGA GCTGGAAGCA 1200
GATCTGGCCG AGCAGCAGCA CCTGCGGCAG CAGGCGGCCG ACGACTGTGA 1250
ATTCCTGCGG GCAGAACTGG ACGAGCTCAG GAGGCAGCGG GAGGACACCG 1300
AGAAGGCTCA GCGGAGCCTG TCTGAGATAG AAAGGAAAGC TCAAGCCAAT 1350
GAACAGCGAT ATAGCAAGCT AAAGGAGAAG TACAGCGAGC TGGTTCAGAA 1400
CCACGCTGAC CTGCTGCGGA AGAATGCAGA GGTGACCAAA CAGGTGTCCA 1450
TGGCCAGACA AGCCCAGGTA GATTTGGAAC GAGAGAAAAA AGAGCTGGAG 1500
GATTCGTTGG AGCGCATCAG TGACCAGGGC CAGCGGAAGA CTCAAGAACA 1550
GCTGGAAGTT CTAGAGAGCT TGAAGCAGGA ACTTGGCACA AGCCAACGGG 1600
AGCTTCAGGT TCTGCAAGGC AGCCTGGAAA CTTCTGCCCA GTCAGAAGCA 1650
AACTGGGCAG CCGAGTTCGC CGAGCTAGAG AAGGAGCGGG ACAGCCTGGT 1700
GAGTGGCGCA GCTCATAGGG AGGAGGAATT ATCTGCTCTT CGGAAAGAAC 1750
TGCAGGACAC TCAGCTCAAA CTGGCCAGCA CAGAGGAATC TATGTGCCAG 1800
CTTGCCAAAG ACCAACGAAA AATGCTTCTG GTGGGGTCCA GGAAGGCTGC 1850
GGAGCAGGTG ATACAAGACG CCCTGAACCA GCTTGAAGAA CCTCCTCTCA 1900
TCAGCTGCGC TGGGTCTGCA GATCACCTCC TCTCCACGGT CACATCCATT 1950
TCCAGCTGCA TCGAGCAACT GGAGAAAAGC TGGAGCCAGT ATCTGGCCTG 2000
CCCAGAAGAC ATCAGTGGAC TTCTCCATTC CATAACCCTG CTGGCCCACT 2050
TGACCAGCGA CGCCATTGCT CATGGTGCCA CCACCTGCCT CAGAGCCCCA 2100
CCTGAGCCTG CCGACTCACT GACCGAGGCC TGTAAGCAGT ATGGCAGGGA 2150
AACCCTCGCC TACCTGGCCT CCCTGGAGGA AGAGGGAAGC CTTGAGAATG 2200
CCGACAGCAC AGCCATGAGG AACTGCCTGA GCAAGATCAA GGCCATCGGC 2250
GAGGAGCTCC TGCCCAGGGG ACTGGACATC AAGCAGGAGG AGCTGGGGGA 2300
CCTGGTGGAC AAGGAGATGG CGGCCACTTC AGCTGCTATT GAAACTTGCA 2350
CGGCCAGAAT AGAGGAGATG CTCAGCAAAT CCCGAGCAGG AGACACAGGA 2400
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GCAAGCTATT CAGGTGCTCA TCGTGGCCTC TAAGGACCTC CAGAGAGAGA 2500
TTGTGGAGAG CGGCAGGGGT ACAGCATCCC CTAAAGAGTT TTATGCCAAG 2550
AACTCTCGAT GGACAGAAGG ACTTATCTCA GCCTCCAAGG CTGTGGGCTG 2600
GGGAGCCACT GTCATGGTGG ATGCAGCTGA TCTGGTGGTA CAAGGCAGAG 2650
GGAAATTTGA GGAGCTAATG GTGTGTTCTC ATGAAATTGC TGCTAGCACA 2700
GCCCAGCTTG TGGCTGCATC CAAGGTGAAA GCTGATAAGG ACAGCCCCAA 2750
CCTAGCCCAG CTGCAGCAGG CCTCTCGGGG AGTGAACCAG GCCACTGCCG 2800
GCGTTGTGGC CTCAACCATT TCCGGCAAAT CACAGATCGA AGAGACAGAC 2850
AACATGGACT TCTCAAGCAT GACGCTGACA CAGATCAAAC GCCAAGAGAT 2900
GGATTCTCAG GTTAGGGTGC TAGAGCTAGA AAATGAATTG CAGAAGGAGC 2950
GTCAAAAACT GGGAGAGCTT CGGAAAAAGC ACTACGAGCT TGCTGGTGTT 3000
GCTGAGGGCT GGGAAGAAGG AACAGAGGCA TCTCCACCTA CACTGCAAGA 3050
AGTGGTAACC GAAAAAGAAT AGAGCCAAAC CAACACCCCA TATGTCAGTG 3100
TAAATCCTTG TTACCTATCT CGTGTGTGTT ATTTCCCCAG CCACAGGCCA 3150
AATCCTTGGA GTCCCAGGGG CAGCCACACC ACTGCCATTA CCCAGTGCCG 3200
AGGACATGCA TGACACTTCC CAAAGATCCC TCCATAGCGA CACCCTTTCT 3250
GTTTGGACCC ATGGTCATCT CTGTTCTTTT CCCGCCTCCC TAGTTAGCAT 3300

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CCAGGCTGGC CAGTGCTGCC CATGAGCAAG CCTAGGTACG AAGAGGGGTG  3350
GTGGGGGGCA GGGCCACTCA ACAGAGAGGA CCAACATCCA GTCCTGCTGA  3400
CTATTTGACC CCCACAACAA TGGGTATCCT TAATAGAGGA GCTGCTTGTT  3450
GTTTGTTGAC AGCTTGGAAA GGGAAGATCT TATGCCTTTT CTTTTCTGTT  3500
TTCTTCTCAG TCTTTTCAGT TTCATCATTT GCACAAACTT GTGAGCATCA  3550
GAGGGCTGAT GGATTCCAAA CCAGGACACT ACCCTGAGAT CTGCACAGTC  3600
AGAAGGACGG CAGGAGTGTC CTGGCTGTGA ATGCCAAAGC CATTCTCCCC  3650
CTCTTTGGGC AGTGCCATGG ATTTCCACTG CTTCTTATGG TGGTTGGTTG  3700
GGTTTTTTGG TTTTGTTTTT TTTTTTTAAG TTTCACTCAC ATAGCCAACT  3750
CTCCCAAAGG GCACACCCCT GGGGCTGAGT CTCCAGGGCC CCCCAACTGT  3800
GGTAGCTCCA GCGATGGTGC TGCCCAGGCC TCTCGGTGCT CCATCTCCGC  3850
CTCCACACTG ACCAAGTGCT GGCCCACCCA GTCCATGCTC CAGGGTCAGG  3900
CGGAGCTGCT GAGTGACAGC TTTCCTCAAA AAGCAGAAGG AGAGTGAGTG  3950
CCTTTCCCTC CTAAAGCTGA ATCCCGGCGG AAAGCCTCTG TCCGCCTTTA  4000
CAAGGGAGAA GACAACAGAA AGAGGGACAA GAGGGTTCAC ACAGCCCAGT  4050
TCCCGTGACG AGGCTCAAAA ACTTGATCAC ATGCTTGAAT GGAGCTGGTG  4100
AGATCAACAA CACTACTTCC CTGCCGGAAT GAACTGTCCG TGAATGGTCT  4150
CTGTCAAGCG GGCCGTCTCC CTTGGCCCAG AGACGGAGTG TGGGAGTGAT  4200
TCCCAACTCC TTTCTGCAGA CGTCTGCCTT GGCATCCTCT TGAATAGGAA  4250
GATCGTTCCA CTTTCTACGC AATTGACAAA CCCGGAAGAT CAGATGCAAT  4300
TGCTCCCATC AGGGAAGAAC CCTATACTTG GTTTGCTACC CTTAGTATTT  4350
ATTACTAACC TCCCTTAAGC AGCAACAGCC TACAAAGAGA TGCTTGGAGC  4400
AATCAGAACT TCAGGTGTGA CTCTAGCAAA GCTCATCTTT CTGCCCGGCT  4450
ACATCAGCCT TCAAGAATCA GAAGAAAGCC AAGGTGCTGG ACTGTTACTG  4500
ACTTGGATCC CAAAGCAAGG AGATCATTTG GAGCTCTTGG GTCAGAGAAA  4550
ATGAGAAAGG ACAGAGCCAG CGGCTCCAAC TCCTTTCAGC CACATGCCCC  4600
AGGCTCTCGC TGCCCTGTGG ACAGGATGAG GACAGAGGGC ACATGAACAG  4650
CTTGCCAGGG ATGGGCAGCC CAACAGCACT TTTCCTCTTC TAGATGGACC  4700
CCAGCATTTA AGTGACCTTC TGATCTTGGG AAAACAGCGT CTTCCTTCTT  4750
TATCTATAGC AACTCATTGG TGGTAGCCAT CAAGCACTTC GGAATT      4796
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(2) INFORMATION FOR SEQ ID NO: 4:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 924
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

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Met Ser Arg Met Trp Gly His Leu Ser Glu Gly Tyr Gly Gln Leu
 1               5                  10                  15

Cys Ser Ile Tyr Leu Lys Leu Leu Arg Thr Lys Met Glu Tyr His
            20                  25                  30
```

Thr Lys Asn Pro Arg Phe Pro Gly Asn Leu Gln Met Ser Asp Arg
35 40 45

Gln Leu Asp Glu Ala Gly Glu Ser Asp Val Asn Asn Phe Phe Gln
50 55 60

Leu Thr Val Glu Met Phe Asp Tyr Leu Glu Cys Glu Leu Asn Leu
65 70 75

Phe Gln Thr Val Phe Asn Ser Leu Asp Met Ser Arg Ser Val Ser
80 85 90

Val Thr Ala Ala Gly Gln Cys Arg Leu Ala Pro Leu Ile Gln Val
95 100 105

Ile Leu Asp Cys Ser His Leu Tyr Asp Tyr Thr Val Lys Leu Leu
110 115 120

Phe Lys Leu His Ser Cys Leu Pro Ala Asp Thr Leu Gln Gly His
125 130 135

Arg Asp Arg Phe Met Glu Gln Phe Thr Lys Leu Lys Asp Leu Phe
140 145 150

Tyr Arg Ser Ser Asn Leu Gln Tyr Phe Lys Arg Leu Ile Gln Ile
155 160 165

Pro Gln Leu Pro Glu Asn Pro Pro Asn Phe Leu Arg Ala Ser Ala
170 175 180

Leu Ser Glu His Ile Ser Pro Val Val Val Ile Pro Ala Glu Ala
185 190 195

Ser Ser Pro Asp Ser Glu Pro Val Leu Glu Lys Asp Asp Leu Met
200 205 210

Asp Met Asp Ala Ser Gln Gln Asn Leu Phe Asp Asn Lys Phe Asp
215 220 225

Asp Ile Phe Gly Ser Ser Phe Ser Ser Asp Pro Phe Asn Phe Asn
230 235 240

Ser Gln Asn Gly Val Asn Lys Asp Glu Lys Asp His Leu Ile Glu
245 250 255

Arg Leu Tyr Arg Glu Ile Ser Gly Leu Lys Ala Gln Leu Glu Asn
260 265 270

Met Lys Thr Glu Ser Gln Arg Val Val Leu Gln Leu Lys Gly His
275 280 285

Val Ser Glu Leu Glu Ala Asp Leu Ala Glu Gln Gln His Leu Arg
290 295 300

Gln Gln Ala Ala Asp Asp Cys Glu Phe Leu Arg Ala Glu Leu Asp
305 310 315

Glu Leu Arg Arg Gln Arg Glu Asp Thr Glu Lys Ala Gln Arg Ser
320 325 330

Leu Ser Glu Ile Glu Arg Lys Ala Gln Ala Asn Glu Gln Arg Tyr
335 340 345

Ser Lys Leu Lys Glu Lys Tyr Ser Glu Leu Val Gln Asn His Ala
350 355 360

Asp Leu Leu Arg Lys Asn Ala Glu Val Thr Lys Gln Val Ser Met
365 370 375

Ala Arg Gln Ala Gln Val Asp Leu Glu Arg Glu Lys Lys Glu Leu
380 385 390

Glu Asp Ser Leu Glu Arg Ile Ser Asp Gln Gly Gln Arg Lys Thr
395 400 405

Gln Glu Gln Leu Glu Val Leu Glu Ser Leu Lys Gln Glu Leu Gly
410 415 420

Thr Ser Gln Arg Glu Leu Gln Val Leu Gln Gly Ser Leu Glu Thr
425 430 435

Ser Ala Gln Ser Glu Ala Asn Trp Ala Ala Glu Phe Ala Glu Leu
440 445 450

Glu Lys Glu Arg Asp Ser Leu Val Ser Gly Ala Ala His Arg Glu
455 460 465

Glu Glu Leu Ser Ala Leu Arg Lys Glu Leu Gln Asp Thr Gln Leu
470 475 480

Lys Leu Ala Ser Thr Glu Glu Ser Met Cys Gln Leu Ala Lys Asp
485 490 495

Gln Arg Lys Met Leu Leu Val Gly Ser Arg Lys Ala Ala Glu Gln
500 505 510

Val Ile Gln Asp Ala Leu Asn Gln Leu Glu Glu Pro Pro Leu Ile
515 520 525

Ser Cys Ala Gly Ser Ala Asp His Leu Leu Ser Thr Val Thr Ser
530 535 540

Ile Ser Ser Cys Ile Glu Gln Leu Glu Lys Ser Trp Ser Gln Tyr
545 550 555

Leu Ala Cys Pro Glu Asp Ile Ser Gly Leu Leu His Ser Ile Thr
560 565 570

Leu Leu Ala His Leu Thr Ser Asp Ala Ile Ala His Gly Ala Thr
575 580 585

Thr Cys Leu Arg Ala Pro Pro Glu Pro Ala Asp Ser Leu Thr Glu
590 595 600

Ala Cys Lys Gln Tyr Gly Arg Glu Thr Leu Ala Tyr Leu Ala Ser
605 610 615

Leu Glu Glu Glu Gly Ser Leu Glu Asn Ala Asp Ser Thr Ala Met
620 625 630

Arg Asn Cys Leu Ser Lys Ile Lys Ala Ile Gly Glu Glu Leu Leu
635 640 645

Pro Arg Gly Leu Asp Ile Lys Gln Glu Glu Leu Gly Asp Leu Val
650 655 660

Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu Thr Cys Thr
665 670 675

Ala Arg Ile Glu Glu Met Leu Ser Lys Ser Arg Ala Gly Asp Thr
680 685 690

Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Arg Cys Cys Thr
695 700 705

Ser Leu Met Gln Ala Ile Gln Val Leu Ile Val Ala Ser Lys Asp
710 715 720

Leu Gln Arg Glu Ile Val Glu Ser Gly Arg Gly Thr Ala Ser Pro
725 730 735

Lys Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu Ile
740 745 750

Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Val Met Val Asp
765 770 775

Ala Ala Asp Leu Val Val Gln Gly Arg Gly Lys Phe Glu Glu Leu
780 785 790

Met Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala Gln Leu Val
795 800 805

```
Ala Ala Ser Lys Val Lys Ala Asp Lys Asp Ser Pro Asn Leu Ala
                  810                 815                 820

Gln Leu Gln Gln Ala Ser Arg Gly Val Asn Gln Ala Thr Ala Gly
                  825                 830                 835

Val Val Ala Ser Thr Ile Ser Gly Lys Ser Gln Ile Glu Glu Thr
                  840                 845                 850

Asp Asn Met Asp Phe Ser Ser Met Thr Leu Thr Gln Ile Lys Arg
                  855                 860                 865

Gln Glu Met Asp Ser Gln Val Arg Val Leu Glu Leu Glu Asn Glu
                  870                 875                 880

Leu Gln Lys Glu Arg Gln Lys Leu Gly Glu Leu Arg Lys Lys His
                  885                 890                 895

Tyr Glu Leu Ala Gly Val Ala Glu Gly Trp Glu Glu Gly Thr Glu
                  900                 905                 910

Ala Ser Pro Pro Thr Leu Gln Glu Val Val Thr Glu Lys Glu
                  915                 920             924
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(2) INFORMATION FOR SEQ ID NO: 5
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1090
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

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Met Leu Leu Cys Gln Gly Ser Glu Trp Arg Arg Asp Gln Gln Leu
                   5                  10                  15

Gly Thr Ala Asn Ala Arg Gln Trp Cys Pro Leu Pro Gln Asp Ala
                  20                  25                  30

Gln Pro Ala Gly Ser Trp Glu Arg Cys Pro Pro Leu Pro Pro Ala
                  35                  40                  45

Gly Arg Leu Gln Gly Thr Asp His Pro Trp Gly Trp Gly Arg Leu
                  50                  55                  60
```

Ala Gly Gly Gly Glu Arg Gly Gly Leu Trp Glu Gly Leu Ser His
65 70 75

Ser Gln Arg Leu Ile His Leu Ile Leu Leu Ser Leu Pro Leu Leu
80 85 90

Val Phe Gln Thr Val Ser Ile Asn Lys Ala Ile Asn Thr Gln Glu
95 100 105

Val Ala Val Lys Glu Lys His Ala Arg Thr Cys Ile Leu Gly Thr
110 115 120

His His Glu Lys Gly Ala Gln Thr Phe Trp Ser Val Val Asn Arg
125 130 135

Leu Pro Leu Ser Ser Asn Ala Val Leu Cys Trp Lys Phe Cys His
140 145 150

Val Phe His Lys Leu Leu Arg Asp Gly His Pro Asn Val Leu Lys
155 160 165

Asp Ser Leu Arg Tyr Arg Asn Glu Leu Ser Asp Met Ser Arg Met
170 175 180

Trp Gly His Leu Ser Glu Gly Tyr Gly Gln Leu Cys Ser Ile Tyr
185 190 195

Leu Lys Leu Leu Arg Thr Lys Met Glu Tyr His Thr Lys Asn Pro
200 205 210

Arg Phe Pro Gly Asn Leu Gln Met Ser Asp Arg Gln Leu Asp Glu
215 220 225

Ala Gly Glu Ser Asp Val Asn Asn Phe Phe Gln Leu Thr Val Glu
230 235 240

Met Phe Asp Tyr Leu Glu Cys Glu Leu Asn Leu Phe Gln Thr Val
245 250 255

Phe Asn Ser Leu Asp Met Ser Arg Ser Val Ser Val Thr Ala Ala
260 265 270

Gly Gln Cys Arg Leu Ala Pro Leu Ile Gln Val Ile Leu Asp Cys
275 288 285

Ser His Leu Tyr Asp Tyr Thr Val Lys Leu Leu Phe Lys Leu His
290 295 300

Ser Cys Leu Pro Ala Asp Thr Leu Gln Gly His Arg Asp Arg Phe
305 310 315

Met Glu Gln Phe Thr Lys Leu Lys Asp Leu Phe Tyr Arg Ser Ser
320 325 330

Asn Leu Gln Tyr Phe Lys Arg Leu Ile Gln Ile Pro Gln Leu Pro
335 340 345

Glu Asn Pro Pro Asn Phe Leu Arg Ala Ser Ala Leu Ser Glu His
350 355 360

Ile Ser Pro Val Val Val Ile Pro Ala Glu Ala Ser Ser Pro Asp
365 370 375

Ser Glu Pro Val Leu Glu Lys Asp Asp Leu Met Asp Met Asp Ala
380 385 390

Ser Gln Gln Asn Leu Phe Asp Asn Lys Phe Asp Asp Ile Phe Gly
395 400 405

Ser Ser Phe Ser Ser Asp Pro Phe Asn Phe Asn Ser Gln Asn Gly
410 415 420

Val Asn Lys Asp Glu Lys Asp His Leu Ile Glu Arg Leu Tyr Arg
425 430 435

Glu Ile Ser Gly Leu Lys Ala Gln Leu Glu Asn Met Lys Thr Glu
440 445 450

Ser Gln Arg Val Val Leu Gln Leu Lys Gly His Val Ser Glu Leu
455 460 465

Glu Ala Asp Leu Ala Glu Gln Gln His Leu Arg Gln Gln Ala Ala
470 475 480

Asp Asp Cys Glu Phe Leu Arg Ala Glu Leu Asp Glu Leu Arg Arg
485 490 495

Gln Arg Glu Asp Thr Glu Lys Ala Gln Arg Ser Leu Ser Glu Ile
500 505 510

Glu Arg Lys Ala Gln Ala Asn Glu Gln Arg Tyr Ser Lys Leu Lys
515 520 525

Glu Lys Tyr Ser Glu Leu Val Gln Asn His Ala Asp Leu Leu Arg
530 535 540

Lys Asn Ala Glu Val Thr Lys Gln Val Ser Met Ala Arg Gln Ala
545 550 555

Gln Val Asp Leu Glu Arg Glu Lys Lys Glu Leu Glu Asp Ser Leu
560 565 570

Glu Arg Ile Ser Asp Gln Gly Gln Arg Lys Thr Gln Glu Gln Leu
575 588 585

Glu Val Leu Glu Ser Leu Lys Gln Glu Leu Ala Thr Ser Gln Arg
590 595 600

Glu Leu Gln Val Leu Gln Gly Ser Leu Glu Thr Ser Ala Gln Ser
605 610 615

Glu Ala Asn Trp Ala Ala Glu Phe Ala Glu Leu Glu Lys Glu Arg
620 625 630

Asp Ser Leu Val Ser Gly Ala Ala His Arg Glu Glu Glu Leu Ser
635 640 645

Ala Leu Arg Lys Glu Leu Gln Asp Thr Gln Leu Lys Leu Ala Ser
650 655 660

Thr Glu Glu Ser Met Cys Gln Leu Ala Lys Asp Gln Arg Lys Met
665 670 675

Leu Leu Val Gly Ser Arg Lys Ala Ala Glu Gln Val Ile Gln Asp
680 685 690

Ala Leu Asn Gln Leu Glu Glu Pro Pro Leu Ile Ser Cys Ala Gly
695 700 705

Ser Ala Asp His Leu Leu Ser Thr Val Thr Ser Ile Ser Ser Cys
710 715 720

Ile Glu Gln Leu Glu Lys Ser Trp Ser Gln Tyr Leu Ala Cys Pro
725 730 735

Glu Asp Ile Ser Gly Leu Leu His Ser Ile Thr Leu Leu Ala His
740 745 750

Leu Thr Ser Asp Ala Ile Ala His Gly Ala Thr Thr Cys Leu Arg
755 760 765

Ala Pro Pro Glu Pro Ala Asp Ser Leu Thr Glu Ala Cys Lys Gln
770 775 780

Tyr Gly Arg Glu Thr Leu Ala Tyr Leu Ala Ser Leu Glu Glu Glu
785 790 795

Gly Ser Leu Glu Asn Ala Asp Ser Thr Ala Met Arg Asn Cys Leu
800 805 810

Ser Lys Ile Lys Ala Ile Gly Glu Glu Leu Leu Pro Arg Gly Leu
815 820 825

Asp Ile Lys Gln Glu Glu Leu Gly Asp Leu Val Asp Lys Glu Met
830 835 840

Ala Ala Thr Ser Ala Ala Ile Glu Thr Ala Thr Ala Arg Ile Glu
845 850 855

Glu Met Leu Ser Lys Ser Arg Ala Gly Asp Thr Gly Val Lys Leu
860 865 870

Glu Val Asn Glu Arg Ile Leu Gly Cys Cys Thr Ser Leu Met Gln
875 888 885

Ala Ile Gln Val Leu Ile Val Ala Ser Lys Asp Leu Gln Arg Glu
890 895 900

Ile Val Glu Ser Gly Arg Gly Thr Ala Ser Pro Lys Glu Phe Tyr
905 910 915

Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu Ile Ser Ala Ser Lys
920 925 930

Ala Val Gly Trp Gly Ala Thr Val Met Val Asp Ala Ala Asp Leu
935 940 945

Val Val Gln Gly Arg Gly Lys Phe Glu Glu Leu Met Val Cys Ser
950 955 960

His Glu Ile Ala Ala Ser Thr Ala Gln Leu Val Ala Ala Ser Lys
965 970 975

Val Lys Ala Asp Lys Asp Ser Pro Asn Leu Ala Gln Leu Gln Gln
980 985 990

Ala Ser Arg Gly Val Asn Gln Ala Thr Ala Gly Val Val Ala Ser
995 1000 1005

Thr Ile Ser Gly Lys Ser Gln Ile Glu Glu Thr Asp Asn Met Asp
1010 1015 1020

Phe Ser Ser Met Thr Leu Thr Gln Ile Lys Arg Gln Glu Met Asp
1025 1030 1035

Ser Gln Val Arg Val Leu Glu Leu Glu Asn Glu Leu Gln Lys Glu
1040 1045 1050

Arg Gln Lys Leu Gly Glu Leu Arg Lys Lys His Tyr Glu Leu Ala
1055 1060 1065

Gly Val Ala Glu Gly Trp Glu Glu Gly Thr Glu Ala Ser Pro Pro
1070 1075 1080

Thr Leu Gln Glu Val Val Thr Glu Lys Glu
1085 1090

(2) INFORMATION FOR SEQ ID NO:6:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3301
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 6:

CGGTGAGCTG GAGGAGCAGC GGAAGCAGAA GCAGAAGGCC CTGGTGGATA 50
ATGAGCAGCT CCGCCACGAG CTGGCCCAGC TGAGGGCTGC CCAGCTGGAG 100
CGCGAGCGGA GCCAGGGCCT GCGTGAGGAG GCTGAGAGGA AGGCCAGTGC 150
CACGGAGGCG CGCTACAACA AGCTGAAGGA AAAGCACAGT GAGCTCGTCC 200
ATGTGCACGC GGAGCTGCTC AGAAAGAACG CGGACACAGC CAAGCAGCTG 250
ACGGTGACGC AGCAAAGCCA GGAGGAGGTG GCGCGGGTGA AGGAGCAGCT 300
GGCCTTCCAG GTGGAGCAGG TGAAGCGGGA GTCGGAGTTG AAGCTAGAGG 350
AGAAGAGCGA CCAGCAGGAG AAGCTCAAGA GGGAGCTGGA GGCCAAGGCC 400
GGAGAGCTGG CCCGCGCGCA GGAGGCCCTG AGCCACACAG AGCAGAGCAA 450
GTCGGAGCTG AGCTCACGGC TGGACACACT GAGTGCGGAG AAGGATGCTC 500
TGAGTGGAGC TGTGCGGCAG CGGGAGGCAG ACCTGCTGGC GGCGCAGAGC 550
CTGGTGCGCG AGACAGAGGC GGCGCTGAGC CGGGAGCAGC AGCGCAGCTC 600
CCAGGAGCAG GGCGAGTTGC AGGGCCGGCT GGCAGAGAGG GAGTCTCAGG 650
AGCAGGGGCT GCGGCAGAGG CTGCTGGACG AGCAGTTCGC AGTGTTGCGG 700
GGCGCTGCTG CCGAGGCCGC GGGCATCCTG CAGGATGCCG TGAGCAAGCT 750
GGACGACCCC CTGCACCTGC GCTGTACCAG CTCCCCAGAC TACCTGGTGA 800
GCAGGGCCCA GGAGGCCTTG GATGCCGTGA GCACCCTGGA GGAGGGCCAC 850
GCCCAGTACC TGACCTCCTT GGCAGACGCC TCCGCCCTGG TGGCAGCTCT 900
GACCCGCTTC TCCCACCTGG CTGCGGATAC CATCATCAAT GGCGGTGCCA 950
CCTCGCACCT GGCTCCCACC GACCCTGCCG ACCGCCTCAT AGACACCTGC 1000
AGGGAGTGCG GGGCCCGGGC TCTGGAGCTC ATGGGGCAGC TGCAGGACCA 1050
GCAGGCTCTG CGGCACATGC AGGCCAGCCT GGTGCGGACA CCCCTGCAGG 1100
GCATCCTTCA GCTGGGCCAA GAACTGAAAC CCAAGAGCCT AGATGTGCGG 1150
CAGGAGGAGC TGGGGGCCGT GGTCGACAAG GAGATGGCGG CCACATCCGC 1200
AGCCATTGAA GATGCTGTGC GGAGGATTGA GGACATGATG AACCAGGCAC 1250
GCCACGCCAG CTCGGGGGTG AAGCTGGAGG TGAACGAGAG GATCCTCAAC 1300
TCCTGCACAG ACCTGATGAA GGCTATCCGG CTCCTGGTGA CGACATCCAC 1350
TAGCCTGCAG AAGGAGATCG TGGAGAGCGG CAGGGGGGCA GCCACGCAGC 1400
AGGAATTTTA CGCCAAGAAC TCGCGCTGGA CCGAAGGCCT CATCTCGGCC 1450
TCCAAGGCTG TGGGCTGGGG AGCCACACAG CTGGTGGAGG CAGCTGACAA 1500
GGTGGTGCTT CACACGGGCA AGTATGAGGA GCTCATCGTC TGCTCCCACG 1550
AGATCGCAGC CAGCACGGCC CAGCTGGTGG CGGCCTCCAA GGTGAAGGCC 1600

```
AACAAGCACA GCCCCCACCT GAGCCGCCTG CAGGAATGTT CTCGCACAGT 1650
CAATGAGAGG GCTGCCAATG TGGTGGCCTC CACCAAGTCA GGCCAGGAGC 1700
AGATTGAGGA CAGAGACACC ATGGATTTCT CCGGCCTGTC CCTCATCAAG 1750
CTGAAGAAGC AGGAGATGGA GACGCAGGTG CGTGTCCTGG AGCTGGAGAA 1800
GACGCTGGAG GCTGAACGCA TGCGGCTGGG GGAGTTGCGG AAGCAACACT 1850
ACGTGCTGGC TGGGGCATCA GGCAGCCCTG GAGAGGAGGT GGCCATCCGG 1900
CCCAGCACTG CCCCCCGAAG TGTAACCACC AAGAAACCAC CCCTGGCCCA 1950
GAAGCCCAGC GTGGCCCCCA GACAGGACCA CCAGCTTGAC AAAAAGGATG 2000
GCATCTACCC AGCTCAACTC GTGAACTACT AGGCCCCCCA GGGGTCCAGC 2050
AGGGTGGCTG GTGACAGGCC TGGGCCTCTG CAACTGCCCT GACAGGACCG 2100
AGAGGCCTTG CCCCTCCACC TGGTGCCCAA GCCTCCCGCC CCACCGTCTG 2150
GATCAATGTC CTCAAGGCCC CTGGCCCTTA CTGAGCCTGC AGGGTCCTGG 2200
GCCATGTGGG TGGTGCTTCT GGATGTGAGT CTCTTATTTA TCTGCAGAAG 2250
GAACTTTGGG GTGCAGCCAG GACCCGGTAG GCCTGAGCCT CAACTCTTCA 2300
GAAAATAGTG TTTTTAATAT TCCTCTTCAG AAAATAGTGT TTTTAATATT 2350
CCGAGCTAGA GCTCTTCTTC CTACGTTTGT AGTCAGCACA CTGGGAAACC 2400
GGGCCAGCGT GGGGCTCCCT GCCTTCTGGA CTCCTGAAGG TCGTGGATGG 2450
ATGGAAGGCA CACAGCCCGT GCCGGCTGAT GGGACGAGGG TCAGGCATCC 2500
TGTCTGTGGC CTTCTGGGGC ACCGATTCTA CCAGGCCCTC CAGCTGCGTG 2550
GTCTCCGCAG ACCAGGCTCT GTGTGGGCTA GAGGAATGTC GCCCATTACC 2600
TCCTCAGGCC CTGGCCCTCG GGCCTCCGTG ATGGGAGCCC CCCAGGAGGG 2700
GTCAGATGCT GGAAGGGGCC GCTTTCTGGG GAGTGAGGTG AGACATAGCG 2750
GCCCAGGCGC TGCCTTCACT CCTGGAGTTT CCATTTCCAG CTGGAATCTG 2800
CAGCCACCCC CATTTCCTGT TTTCCATTCC CCCGTTCTGG CCGCGCCCCA 2850
CTGCCCACCT GAAGGGGTGG TTTCCAGCCC TCCGGAGAGT GGGCTTGGCC 2900
CTAGGCCCTC CAGCTCAGCC AGAAAAAGCC CAGAAACCCA GGTGCTGGAC 2950
CAGGGCCCTC AGGGAGGGAC CCTGCGGCTA GAGTGGGCTA GGCCCTGGCT 3000
TTGCCCGTCA GATTTGAACG AATGTGTGTC CCTTGAGCCC AAGGAGAGCG 3050
GCAGGAGGGG TGGGACCAGG CTGGGAGGAC AGAGCCAGCA GCTGCCATGC 3100
CCTCCTGCTC CCCCCACCCC AGCCCTAGCC CTTTAGCCTT TCACCCTGTG 3150
CTCTGGAAAG GCTACCAAAT ACTGGCCAAG GTCAGGAGGA GCAAAAATGA 3200
GCCAGCACCA GCGCCTTGGC TTTGTGTTAG CATTTCCTCC TGAAGTGTTC 3250
TGTTGGCAAT AAAATGCACT TTGACTGTTA AAAAAAAAAA AAAAAAAAAA 3300
A                                                       3301
```

(2) INFORMATION FOR SEQ ID NO: 7

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 676

(B) TYPE: protein

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: protein

(iii) HYPOTHETICAL: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(ix) FEATURE: Huntingtin-interacting protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

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Gly Glu Leu Glu Glu Gln Arg Lys Gln Lys Gln Lys Ala Leu Val
 5                  10                  15
```

Asp Asn Glu Gln Leu Arg His Glu Leu Ala Gln Leu Arg Ala Ala
20 25 30

Gln Leu Glu Arg Glu Arg Ser Gln Gly Leu Arg Glu Glu Ala Glu
35 40 45

Arg Lys Ala Ser Ala Thr Glu Ala Arg Tyr Asn Lys Leu Lys Glu
50 55 60

Lys His Ser Glu Leu Val His Val His Ala Glu Leu Leu Arg Lys
65 70 75

Asn Ala Asp Thr Ala Lys Gln Leu Thr Val Thr Gln Gln Ser Gln
80 85 90

Glu Glu Val Ala Arg Val Lys Glu Gln Leu Ala Phe Gln Val Glu
95 100 105

Gln Val Lys Arg Glu Ser Glu Leu Lys Leu Glu Glu Lys Ser Asp
110 115 120

Gln Gln Glu Lys Leu Lys Arg Glu Leu Glu Ala Lys Ala Gly Glu
125 130 135

Leu Ala Arg Ala Gln Glu Ala Leu Ser His Thr Glu Gln Ser Lys
140 145 150

Ser Glu Leu Ser Ser Arg Leu Asp Thr Leu Ser Ala Glu Lys Asp
155 160 165

Ala Leu Ser Gly Ala Val Arg Gln Arg Glu Ala Asp Leu Leu Ala
170 175 180

Ala Gln Ser Leu Val Arg Glu Thr Glu Ala Ala Leu Ser Arg Glu
185 190 195

Gln Gln Arg Ser Ser Gln Glu Gln Gly Glu Leu Gln Gly Arg Leu
200 205 210

Ala Glu Arg Glu Ser Gln Glu Gln Gly Leu Arg Gln Arg Leu Leu
215 220 225

Asp Glu Gln Phe Ala Val Leu Arg Gly Ala Ala Ala Glu Ala Ala
230 235 240

Gly Ile Leu Gln Asp Ala Val Ser Lys Leu Asp Asp Pro Leu His
245 250 255

Leu Arg Cys Thr Ser Ser Pro Asp Tyr Leu Val Ser Arg Ala Gln
260 265 270

Glu Ala Leu Asp Ala Val Ser Thr Leu Glu Glu Gly His Ala Gln
275 288 285

Tyr Leu Thr Ser Leu Ala Asp Ala Ser Ala Leu Val Ala Ala Leu
290 295 300

Thr Arg Phe Ser His Leu Ala Ala Asp Thr Ile Ile Asn Gly Gly
305 310 315

Ala Thr Ser His Leu Ala Pro Thr Asp Pro Ala Asp Arg Leu Ile
320 325 330

Asp Thr Cys Arg Glu Cys Gly Ala Arg Ala Leu Glu Leu Met Gly
335 340 345

Gln Leu Gln Asp Gln Gln Ala Leu Arg His Met Gln Ala Ser Leu
350 355 360

Val Arg Thr Pro Leu Gln Gly Ile Leu Gln Leu Gly Gln Glu Leu
365 370 375

Lys Pro Lys Ser Leu Asp Val Arg Gln Glu Glu Leu Gly Ala Val
380 385 390

Val Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu Asp Ala
395 400 405

Val Arg Arg Ile Glu Asp Met Met Asn Gln Ala Arg His Ala Ser
410 415 420

Ser Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Asn Ser Cys
425 430 435

Thr Asp Leu Met Lys Ala Ile Arg Leu Leu Val Thr Thr Ser Thr
440 445 450

Ser Leu Gln Lys Glu Ile Val Glu Ser Gly Arg Gly Ala Ala Thr
455 460 465

Gln Gln Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu
470 475 480

Ile Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Gln Leu Val
485 490 495

Glu Ala Ala Asp Lys Val Val Leu His Thr Gly Lys Tyr Glu Glu
500 505 510

Leu Ile Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala Gln Leu
515 520 525

```
Val Ala Ala Ser Lys Val Lys Ala Asn Lys His Ser Pro His Leu
                530                 535                 540

Ser Arg Leu Gln Glu Cys Ser Arg Thr Val Asn Glu Arg Ala Ala
                545                 550                 555

Asn Val Val Ala Ser Thr Lys Ser Gly Gln Glu Gln Ile Glu Asp
                560                 565                 570

Arg Asp Thr Met Asp Phe Ser Gly Leu Ser Leu Ile Lys Leu Lys
                575                 588                 585

Lys Gln Glu Met Glu Thr Gln Val Arg Val Leu Glu Leu Glu Lys
                590                 595                 600

Thr Leu Glu Ala Glu Arg Met Arg Leu Gly Glu Leu Arg Lys Gln
                605                 610                 615

His Tyr Val Leu Ala Gly Ala Ser Gly Ser Pro Gly Glu Glu Val
                620                 625                 630

Ala Ile Arg Pro Ser Thr Ala Pro Arg Ser Val Thr Thr Lys Lys
                635                 640                 645

Pro Pro Leu Ala Gln Lys Pro Ser Val Ala Pro Arg Gln Asp His
                650                 655                 660

Gln Leu Asp Lys Lys Asp Gly Ile Tyr Pro Ala Gln Leu Val Asn
                665                 670                 675

Tyr
```

(2) INFORMATION FOR SEQ ID NO:8:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2338
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: cDNA for Huntingtin-interacting protein - mHIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 8:

```
GGCACGAGGG CTCATTCAGA TCCCCCAGCT GCCCGAGAAT CCACCCAACTT   50
CCTACGAGCC TCGGCCCTGT CAGAGCACAT CAGTCCTGTG GTGGTGATCCC  100
GGCAGAGGTG TCATCCCCAG ACAGTGAGCC TGTCCTGGAG AAGGATGACCT  150
CATGGACATG GACGCCTCCC AGCAGACTTT GTTTGACAAC AAGTTTGATGA  200
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```
CGTCTTTGGC AGCTCATTGA GCAGCGACCC TTTCAATTTC AACAATCAAAA  250
TGGCGTGAAC AAGGACGAGA AGGACCACTT GATTGAACGC CTGTACAGAGA  300
GATCAGTGGA CTGACAGGGC AGCTGGACAA CATGAAGATT GAGAGCCAGCG  350
GGCCATGCTG CAGCTGAAGG GTCGAGTGAG TGAGCTGGAG GCAGAGCTAGC  400
AGAGCAGCAG CACTTGGGCC GGCAGGCTAT GGATGACTGC GAGTTCCTGCG  450
CACTGAGCTG GATGAACTGA AGAGGCAGCG AGAGGACACG GAGAAGGCACA  500
GCGCAGCCTG ACTGAGATAG AAAGAAAGGC CCAGGCTAAT GAACAGAGGTA  550
TAGCAAGTTA AAAGAGAAGT ACAGTGAACT GGTGCAGAAC CATGCTGACCT  600
GCTGCGGAAG AACGCAGAGG TGACCAAACA GGTGTCCGTG GCCCGGCAAGC  650
CCAGGTGGAT TTGGAAAGAG AGAAAAAAGA GCTAGCAGAT TCCTTTGCAC  700
GTGTAAGTGA CCAGGCCCAG CGGAAGACTC AAGAGCAACA GGATGTTCTA  750
GAGAACCTGA AGCATGAACT GGCCACCAGC AGACAGGAGC TGCAGGTCCT  800
CCACAGCAAC CTGGAAACCT CTGCCCAGTC AGAAGCGAAA TGGCTGACAC  850
AGATCGCCGA GTTGGAGAAG GAACAAGGCA GCTTGGCGAC TGTTGCAGCT  900
CAGAGAGAGG AAGAGTTATC AGCCCTCCGA GACCAGCTGG AAAGCACCCA  950
GATCAAGCTG GCTGGGGCCC AGGAATCCAT GTGCCAGCAG GTGAAGGACC 1000
AGAGGAAAAC CCTCTTGGCA GGGATCAGGA AGGCTGCGGA GCGTGAGATA 1050
CAGGAGGCGC TGAGCCAGCT TGAGGAACCC ACCCTCATCA GCTGTGCAGG 1100
ATCCACAGAT CACCTTCTCT CCAAAGTCAG CTCCGTTTCC AGCTGCCTCG 1150
AGCAACTGGA AAAGAACGGC AGCCAGTATC TGGCCTGCCC AGAAGATATT 1200
AGTGAGCTTC TGCACTCGAT CACCCTGCTT GCCCACTTGA CCGGTGACAC 1250
TGTCATCCAG GGGAGTGCCA CCAGCCTCCG GGCCCCACCG GAGCCAGCCG 1300
ACTCGTTGAC GGAGGCCTGT AGGCAGTATG GCAGAGAAAC CCTGGCCTAT 1350
CTGTCCTCCC TGGAGGAAGA GGGAACTGTG GAGAATGCTG ACGTCACAGC 1400
CCTTAGGAAT TGCCTCAGCA GGGTCAAGAC CCTTGGCGAG GAGCTGCTGC 1450
CCAGGGGCCT GGACATCAAG CAGGAAGAGC TGGGTGACCT GGTGGACAAG 1500
GAGATGGCAG CCACTTCAGC TGCCATTGAA GCTGCCACCA CCCGGATAGA 1550
GGAAATTCTC AGTAAGTCCC GAGCAGGAGA CACGGGAGTC AAGCTGGAGG 1600
TGAATGAGAG GATCCTGGGT TCCTGTACCA GCCTGATGCA GGCCATCAAG 1650
GTGCTCGTTG TGGCCTCCAA GGACCTCCAG AAGGAGATAG TGGAGAGTGG 1700
CAGGGGTAGT GCATCCCCTA AAGAATTTTA CGCCAAGAAC TCTCGGTGGA 1750
CGGAAGGGCT GATATCCGCC TCCAAAGCTG TTGGTTGGGG AGCTACCATC 1800
ATGGTGGATG CTGCTGATCT TGTGGTCCAA GGCAAAGGGA AGTTCGAGGA 1850
GCTGATGGTG TGTTCACGCG AGATTGCTGC CAGTACTGCC CAGCTCGTGG 1900
CTGCATCCAA GGTGAAAGCG AACAAGGGCA GCCTCAATCT GACCCAGCTG 2000
CAGCAGGCCT CTCGAGGAGT GAACCAGGCC ACAGCCGCTG TGGTGGCCTC 2050
AACCATTTCT GGCAAATCTC AGATTGAGGA AACAGACAGT ATGGACTTCT 2100
CAAGCATGAC ACTGACCCAG ATCAAGCGCC AGGAGATGGA TTCCCAGGTT 2150
AGGGTGCTGG AGCTGGAAAA TGACCTGCAG AAGGAGCGTC AGAAACTAGG 2200
AGAGCTACGG AAGAAACACT ACGAGCTGGA GGGCGTGGCT GAGGGCTGGG 2250
AGGAAGGGAC AGAAGCATCA CCGTCTACTG TCCAAGAAGC AATACCGGAC 2300
AAAGAGTAGA GCCAAGCCGA CACCCCACAC ATCAGAAA              2338
```

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 676

(B) TYPE: protein

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: protein

(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

```
Ala Arg Gly Leu Ile Gln Ile Pro Gln Leu Pro Glu Asn Pro Pro
                  5                  10                  15

Asn Phe Leu Arg Ala Ser Ala Leu Ser Glu His Ile Ser Pro Val
                 20                  25                  30

Val Val Ile Pro Ala Glu Val Ser Ser Pro Asp Ser Glu Pro Val
                 35                  40                  45

Leu Glu Lys Asp Asp Leu Met Asp Met Asp Ala Ser Gln Gln Thr
                 50                  55                  60

Leu Phe Asp Asn Lys Phe Asp Asp Val Phe Gly Ser Ser Leu Ser
                 65                  70                  75

Ser Asp Pro Phe Asn Phe Asn Asn Gln Asn Gly Val Asn Lys Asp
                 80                  85                  90

Glu Lys Asp His Leu Ile Glu Arg Leu Tyr Arg Glu Ile Ser Gly
                 95                 100                 105

Leu Thr Gly Gln Leu Asp Asn Met Lys Ile Glu Ser Gln Arg Ala
                110                 115                 120

Met Leu Gln Leu Lys Gly Arg Val Ser Glu Leu Glu Ala Glu Leu
                125                 130                 135

Ala Glu Gln Gln His Leu Gly Arg Gln Ala Met Asp Asp Cys Glu
                140                 145                 150

Phe Leu Arg Thr Glu Leu Asp Glu Leu Lys Arg Gln Arg Glu Asp
                155                 160                 165

Thr Glu Lys Ala Gln Arg Ser Leu Thr Glu Ile Glu Arg Lys Ala
                170                 175                 180

Gln Ala Asn Glu Gln Arg Tyr Ser Lys Leu Lys Glu Lys Tyr Ser
                185                 190                 195

Glu Leu Val Gln Asn His Ala Asp Leu Leu Arg Lys Asn Ala Glu
                200                 205                 210

Val Thr Lys Gln Val Ser Val Ala Arg Gln Ala Gln Val Asp Leu
                215                 220                 225

Glu Arg Glu Lys Lys Glu Leu Ala Asp Ser Phe Ala Arg Val Ser
```

230 235 240

Asp Gln Ala Gln Arg Lys Thr Gln Glu Gln Gln Asp Val Leu Glu
245 250 255

Asn Leu Lys His Glu Leu Ala Thr Ser Arg Gln Glu Leu Gln Val
260 265 270

Leu His Ser Asn Leu Glu Thr Ser Ala Gln Ser Glu Ala Lys Trp
275 288 285

Leu Thr Gln Ile Ala Glu Leu Glu Lys Glu Gln Gly Ser Leu Ala
290 295 300

Thr Val Ala Ala Gln Arg Glu Glu Glu Leu Ser Ala Leu Arg Asp
305 310 315

Gln Leu Glu Ser Thr Gln Ile Lys Leu Ala Gly Ala Gln Glu Ser
320 325 330

Met Cys Gln Gln Val Lys Asp Gln Arg Lys Thr Leu Leu Ala Gly
335 340 345

Ile Arg Lys Ala Ala Glu Arg Glu Ile Gln Glu Ala Leu Ser Gln
350 355 360

Leu Glu Glu Pro Thr Leu Ile Ser Cys Ala Gly Ser Thr Asp His
365 370 375

Leu Leu Ser Lys Val Ser Ser Val Ser Ser Cys Leu Glu Gln Leu
380 385 390

Glu Lys Asn Gly Ser Gln Tyr Leu Ala Cys Pro Glu Asp Ile Ser
395 400 405

Glu Leu Leu His Ser Ile Thr Leu Leu Ala His Leu Thr Gly Asp
410 415 420

Thr Val Ile Gln Gly Ser Ala Thr Ser Leu Arg Ala Pro Pro Glu
425 430 435

Pro Ala Asp Ser Leu Thr Glu Ala Cys Arg Gln Tyr Gly Arg Glu
440 445 450

Thr Leu Ala Tyr Leu Ser Ser Leu Glu Glu Glu Gly Thr Val Glu
455 460 465

Asn Ala Asp Val Thr Ala Leu Arg Asn Cys Leu Ser Arg Val Lys
470 475 480

Thr Leu Gly Glu Glu Leu Leu Pro Arg Gly Leu Asp Ile Lys Gln
485 490 495

Glu Glu Leu Gly Asp Leu Val Asp Lys Glu Met Ala Ala Thr Ser
500 505 510

Ala Ala Ile Glu Ala Ala Thr Thr Arg Ile Glu Glu Ile Leu Ser
515 520 525

Lys Ser Arg Ala Gly Asp Thr Gly Val Lys Leu Glu Val Asn Glu
530 535 540

Arg Ile Leu Gly Ser Cys Thr Ser Leu Met Gln Ala Ile Lys Val
545 550 555

Leu Val Val Ala Ser Lys Asp Leu Gln Lys Glu Ile Val Glu Ser
560 565 570

Gly Arg Gly Ser Ala Ser Pro Lys Glu Phe Tyr Ala Lys Asn Ser
575 588 585

Arg Trp Thr Glu Gly Leu Ile Ser Ala Ser Lys Ala Val Gly Trp
590 595 600

Gly Ala Thr Ile Met Val Asp Ala Ala Asp Leu Val Val Gln Gly
605 610 615

Lys Gly Lys Phe Glu Glu Leu Met Val Cys Ser Arg Glu Ile Ala
620 625 630

Ala Ser Thr Ala Gln Leu Val Ala Ala Ser Lys Val Lys Ala Asn
635 640 645

Lys Gly Ser Leu Asn Leu Thr Gln Leu Gln Gln Ala Ser Arg Gly
650 655 660

Val Asn Gln Ala Thr Ala Ala Val Val Ala Ser Thr Ile Ser Gly
665 670 675

Lys Ser Gln Ile Glu Glu Thr Asp Ser Met Asp Phe Ser Ser Met
680 685 690

Thr Leu Thr Gln Ile Lys Arg Gln Glu Met Asp Ser Gln Val Arg
695 700 705

Val Leu Glu Leu Glu Asn Asp Leu Gln Lys Glu Arg Gln Lys Leu
710 715 720

Gly Glu Leu Arg Lys Lys His Tyr Glu Leu Glu Gly Val Ala Glu
725 730 735

```
Gly Trp Glu Glu Gly Thr Glu Ala Ser Pro Ser Thr Val Gln Glu
                740                 745                 750

Ala Ile Pro Asp Lys Glu
                755
```

(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3964
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: cDNA for Huntingtin-interacting protein - mHIP1a
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 10:

```
GGCACGAGGC GGCGCGCGGC CTCCGTGTGC CTAGGCTTGA GGCGGGCGGT   50
GACGCCTCAT TCGCGCGGAG CCGGGCCGGG ACACGGTCGG CGGCAGCATG  100
AACAGCATCA AGAATGTGCC GGCGCGGGTG CTGAGCCGCA GGCCGGGCCA  150
CAGCCTAGAG GCCGAGCGCG AGCAGTTCGA CAAGACGCAG GCCATCAGTA  200
TCAGCAAAGC CATCAACAGC CAGGAGGCCC CAGTGAAGGA GAAGCATGCC  250
CGGCGTATCA TCCTGGGCAC GCATCATGAG AAGGGAGCCT TCACCTTCTG  300
GTCCTATGCC ATCGGCCTGC CGCTGTCCAG CAGCTCCATC CTCAGCTGGA  350
AGTTCTGTCA CGTCCTTCAC AAGGTCCTCC GGGACGGACA CCCCAACGTC  400
CTGCATGACT ATCAGCGGTA CCGGAGCAAC ATACGTGAGA TCGGTGACTT  450
GTGGGGCCAC CTTCGTGACC AGTATGGACA CCTGGTGAAT ATCTATACCA  500
AACTGTTGCT GACTAAGATC TCCTTCCACC TTAAGCACCC CCAGTTTCCT  550
GCAGGCCTGG AGGTAACAGA TGAGGTGTTG GAGAAGGCGG CGGGAACTGA  600
TGTCAACAAC ATTTTTCAGC TTACCGTGGA GATGTTTGAC TACATGGACT  650
GTGAACTGAA GCTTTCTGAG TCAGTTTTCC GGCAGCTCAA CACGGCCATC  700
GCAGTGTCCC AGATGTCTTC TGGCCAGTGT CGCCTAGCGC CGCTCATCCA  750
GGTCATTCAG GACTGCAGCC ACCTGTACCA CTACACAGTG AAGCTCATGT  800
TTAAGCTGCA CTCCTGTCTC CCGGCAGACA CCCTGCAAGG CCACAGGGAT  850
CGGTTCCACG AGCAGTTCCA CAGCCTCAAA AACTTCTTCC GCCGGGCTTC  900
AGACATGCTG TACTTCAAGA GGCTCATCCA GATCCCGCGG CTGCCTGAGG  950
GACCCCCCAA TTTCCTGCGG GCTTCAGCCC TGGCTGAGCA CATCAAGCCG 1000
GTGGTGGTGA TTCCCGAGGA GGCCCCAGAG GAAGAGGAGC CTGAGAACCT 1050
AATTGAAATC AGCAGTGCGC CCCCTGCTGG GGAGCCAGTG GTGGTGGCTG 1100
ACCTCTTTGA TCAGACCTTT GGACCCCCCA ATGGCTCCAT GAAGGATGAC 1150
AGGGACCTCC AAATCGAGAA CTTGAAGAGA GAGGTGGAGA CCCTCCGTGC 1200
TGAGCTGGAG AAGATTAAGA TGGAGGCACA GCGGTACATC TCCCAGCTGA 1250
AGGGCCAGGT GAATGGCCTG GAGGCAGAGC TGGAGGAGCA GCGCAAGCAG 1300
AAGCAGAAGG CCCTGGTGGA CAACGAGCAG CTGCGCCACG AGCTGGCCCA 1350
GCTCAAGGCC CTGCAGCTGG AGGGCGCCCG CAACCAGGGC CTTCGAGAGG 1400
AAGCAGAGAG GAAGGCCAGT GCCACGGAGG CACGCTACAG CAAGCTGAAG 1450
GAGAAACACA GCGAACTCAT TAACACGCAC GCCGAGCTGC TCAGGAAGAA 1500
```

CGCAGACACG GCCAAGCAGC TGACAGTGAC ACAGCAGAGC CAGGAGGAGG 1550
TGGCACGGGT AAAGGAACAG CTGGCCTTCC AGATGGAGCA AGCGAAGCGT 1600
GAGTCTGAGA TGAAGATGGA AGAGCAGAGC GACCAGTTGG AGAAGCTCAA 1650
GAGGGAGCTG GCGGCCAGGG CAGGAGAGCT GGCCCGTGCG CAGGAGGCCC 1700
TGAGCCGCAC AGAACAGAGT GGGTCAGAGC TGAGCTCACG GCTGGACACA 1750
CTGAACGCGG AGAAGGAAGC CCTGAGTGGA GTCGTTCGGC AGCGTGAGGC 1800
AGAGCTGCTG GCCGCTCAGA GCCTGGTGCG GGAGAAGGAG GAGGCGCTTA 1850
GCCAAGAGCA GCAGCGGAGC TCCCAGGAGA AGGGCGAGCT ACGGGGGCAG 1900
CTGGCAGAAA AGGAGTCTCA GGAGCAGGGG CTTCGGCAGA AGCTGCTGGA 1950
TGAGCAGTTG GCGGTGTTGC GAAGTGCAGC CGCCGAGGCA GAGGCCATCC 2000
TACAGGATGC AGTGAGCAAG CTGGACGACC CCCTGCACCT CCGCTGCACC 2050
AGCTCCCCAG ACTACTTGGT GAGCCGGGCT CAGGCAGCCC TGGACAGCGT 2100
GAGCGGCCTG GAGCAGGGCC ACACCCAGTA CCTGGCTTCC TCCGAAGATG 2150
CTTCTGCCCT GGTGGCAGCG CTGACCCGCT TCTCCCATTT GGCTGCGGAC 2200
ACCATTGTCA ATGGTGCCGC CACCTCCCAC CTGGCCCCCA CCGACCCCGC 2250
CGACCGCCTG ATGGACACAT GCAGGGAGTG TGGAGCCCGG GCTCTGGAGC 2300
TGGTGGGACA GCTGCAAGAC CAGACAGTGC TACGGAGGGC TCAGCCCAGC 2350
CTGATGCGGG CCCCCCTGCA GGGCATTCTG CAGTTGGGCC AGGACTTGAA 2400
GCCTAAGAGC CTGGATGTAC GGCAAGAGGA GCTAGGGGCC ATGGTGGACA 2450
AGGAGATGGC GGCCACCTCG GCAGCCATTG AGGACGCTGT GCGGAGGATC 2500
GAGGACATGA TGAGCCAGGC CCGCCACGAG AGCTCAGGCG TGAAACTGGA 2550
GGTGAATGAG AGGATCCTCA ACTCCTGCAC AGACCTGATG AAGGCTATCC 2600
GGCTCCTGGT GATGACCTCC ACCAGCCTGC AGAAGGAAAT TGTGGAGAGC 2650
GGCAGGGGGG CAGCAACGCA GCAGGAATTT TATGCCAAGA ATTCACGGTG 2700
GACTGAAGGC CTCATCTCAG CCTCTAAGGC AGTGGGCTGG GGAGCCACAC 2750
AGCTGGTGGA GTCAGCTGAC AAGGTTGTGC TTCACATGGG CAAATACGAG 2800
GAACTCATCG TCTGCTCCCA TGAGATTGCG GCCAGCACGG CCCAGCTGGT 2850
GGCAGCCTCG AAGGTGAAAG CCAACAAGAA CAGTCCCCAC TTGAGCCGCC 2900
TGCAGGAATG TTCCCGCACT GTCAACGAGA GGGCTGCCAA CGTCGTGGCC 2950
TCCACCAAAT CTGGCCAGGA GCAGATTGAG GACAGAGACA CCATGGATTT 3000
CTCTGGCCTG TCCCTCATCA AGTTGAAGAA GCAGGAGATG GAGACACAGG 3050
TGCGAGTCTT GGAGCTGGAG AAGACACTAG AGGCAGAGCG TGTCCGGCTC 3100
GGGGAGCTTC GGAAACAGCA CTATGTACTG GCTGGGGGGA TGGGAACACC 3150
TAGCGAAGAA GAACCCAGCA GACCCAGCCC AGCTCCCCGA AGTGGGGCCA 3200
CTAAGAAGCC ACCGCTGGCC CAGAAACCCA GCATAGCCCC CAGGACAGAC 3250
AACCAGCTCGA CAAAAAGGAT GGTGTCTACC CAGCTCAACT TGTGAACTAC 3300
TAGGCCCCTAA GGTGTTCAGC AGGATGGCTG GTGGTTGTGC CTGGGCTTCA 3350
TGTGGCTGTCT GGCAGTGGTC AAGGGGCCTC TGAGAAGCCT CCAACTCCTG 3400
CCCAAGGGGCC TAGTCTGTGG GACAGTTCAT CTGGATGTGA ATCTATTTAT 3450
CTTAAGTAGGA ACTGCCTCGA GCAGCTGGGA CCCAGCAGGC CTGAGCCACA 3500
AATCTGCAGCG GACATCAGAG ATAGTCTGAA TGCTGCGAGG TATTTCTTTC 3550
TTCGTAAGTTT AGTCAGCACA CTGGGAAAAG GTCACATAAG CCAGGAGCCT 3600
CCTTGTCTCTG GACTCAAAAG TCTGAGGCCT TAAGTGAACA ACAGAAAGAG 3650
GGTCCCTGCTG GCTACCAGGG ATAAGGGGAT GACCTGTGAC CCTTGAGCCA 3700
GGGAGAGCAGG TAAGCTGGGT GGTGTCATCA CCTGGGGGCC TGGTGCTAGG 3750
GCATCCATGCT GGGAGCCCCA GGAGACCAGG CTTTGTGTGG GAGCCTGGCA 3800
TCATCGTGGCT GGGGCAGCCC CTGCTCAGGT GCTGTCTCTG CCCGTGACCT 3850
TGAAGCCACCC TCCCCCCGTA CAGTTTTCCA TTCTCCTGGC TACTAGTGTG 3900
GCTGTTCATTG CCTACCTTGA TGAGTAGATT TCAGCCCTCC TAAAGCTGGG 3950
GCCTTTCCTCG TGCC 3964

(2) INFORMATION FOR SEQ ID NO: 11:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 676
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: Huntingtin-interacting protein -mHIP1a
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

```
Met Asn Ser Ile Lys Asn Val Pro Ala Arg Val Leu Ser Arg Arg
                  5                  10                  15

Pro Gly His Ser Leu Glu Ala Glu Arg Glu Gln Phe Asp Lys Thr
                 20                  25                  30

Gln Ala Ile Ser Ile Ser Lys Ala Ile Asn Ser Gln Glu Ala Pro
                 35                  40                  45

Val Lys Glu Lys His Ala Arg Arg Ile Ile Leu Gly Thr His His
                 50                  55                  60

Glu Lys Gly Ala Phe Thr Phe Trp Ser Tyr Ala Ile Gly Leu Pro
                 65                  70                  75

Leu Ser Ser Ser Ser Ile Leu Ser Trp Lys Phe Cys His Val Leu
                 80                  85                  90

His Lys Val Leu Arg Asp Gly His Pro Asn Val Leu His Asp Tyr
                 95                 100                 105

Gln Arg Tyr Arg Ser Asn Ile Arg Glu Ile Gly Asp Leu Trp Gly
                110                 115                 120

His Leu Arg Asp Gln Tyr Gly His Leu Val Asn Ile Tyr Thr Lys
                125                 130                 135

Leu Leu Leu Thr Lys Ile Ser Phe His Leu Lys His Pro Gln Phe
                140                 145                 150

Pro Ala Gly Leu Glu Val Thr Asp Glu Val Leu Glu Lys Ala Ala
                155                 160                 165

Gly Thr Asp Val Asn Asn Ile Phe Gln Leu Thr Val Glu Met Phe
                170                 175                 180

Asp Tyr Met Asp Cys Glu Leu Lys Leu Ser Glu Ser Val Phe Arg
```

185 190 195

Gln Leu Asn Thr Ala Ile Ala Val Ser Gln Met Ser Ser Gly Gln
200 205 210

Cys Arg Leu Ala Pro Leu Ile Gln Val Ile Gln Asp Cys Ser His
215 220 225

Leu Tyr His Tyr Thr Val Lys Leu Met Phe Lys Leu His Ser Cys
230 235 240

Leu Pro Ala Asp Thr Leu Gln Gly His Arg Asp Arg Phe His Glu
245 250 255

Gln Phe His Ser Leu Lys Asn Phe Phe Arg Arg Ala Ser Asp Met
260 265 270

Leu Tyr Phe Lys Arg Leu Ile Gln Ile Pro Arg Leu Pro Glu Gly
275 288 285

Pro Pro Asn Phe Leu Arg Ala Ser Ala Leu Ala Glu His Ile Lys
290 295 300

Pro Val Val Val Ile Pro Glu Glu Ala Pro Glu Glu Glu Glu Pro
305 310 315

Glu Asn Leu Ile Glu Ile Ser Ser Ala Pro Pro Ala Gly Glu Pro
320 325 330

Val Val Val Ala Asp Leu Phe Asp Gln Thr Phe Gly Pro Pro Asn
335 340 345

Gly Ser Met Lys Asp Asp Arg Asp Leu Gln Ile Glu Asn Leu Lys
350 355 360

Arg Glu Val Glu Thr Leu Arg Ala Glu Leu Glu Lys Ile Lys Met
365 370 375

Glu Ala Gln Arg Tyr Ile Ser Gln Leu Lys Gly Gln Val Asn Gly
380 385 390

Leu Glu Ala Glu Leu Glu Glu Gln Arg Lys Gln Lys Gln Lys Ala
395 400 405

Leu Val Asp Asn Glu Gln Leu Arg His Glu Leu Ala Gln Leu Lys
410 415 420

Ala Leu Gln Leu Glu Gly Ala Arg Asn Gln Gly Leu Arg Glu Glu
425 430 435

Ala Glu Arg Lys Ala Ser Ala Thr Glu Ala Arg Tyr Ser Lys Leu

440 445 450

Lys Glu Lys His Ser Glu Leu Ile Asn Thr His Ala Glu Leu Leu
455 460 465

Arg Lys Asn Ala Asp Thr Ala Lys Gln Leu Thr Val Thr Gln Gln
470 475 480

Ser Gln Glu Glu Val Ala Arg Val Lys Glu Gln Leu Ala Phe Gln
485 490 495

Met Glu Gln Ala Lys Arg Glu Ser Glu Met Lys Met Glu Glu Gln
500 505 510

Ser Asp Gln Leu Glu Lys Leu Lys Arg Glu Leu Ala Ala Arg Ala
515 520 525

Gly Glu Leu Ala Arg Ala Gln Glu Ala Leu Ser Arg Thr Glu Gln
530 535 540

Ser Gly Ser Glu Leu Ser Ser Arg Leu Asp Thr Leu Asn Ala Glu
545 550 555

Lys Glu Ala Leu Ser Gly Val Val Arg Gln Arg Glu Ala Glu Leu
560 565 570

Leu Ala Ala Gln Ser Leu Val Arg Glu Lys Glu Glu Ala Leu Ser
575 588 585

Gln Glu Gln Gln Arg Ser Ser Gln Glu Lys Gly Glu Leu Arg Gly
590 595 600

Gln Leu Ala Glu Lys Glu Ser Gln Glu Gln Gly Leu Arg Gln Lys
605 610 615

Leu Leu Asp Glu Gln Leu Ala Val Leu Arg Ser Ala Ala Ala Glu
620 625 630

Ala Glu Ala Ile Leu Gln Asp Ala Val Ser Lys Leu Asp Asp Pro
635 640 645

Leu His Leu Arg Cys Thr Ser Ser Pro Asp Tyr Leu Val Ser Arg
650 655 660

Ala Gln Ala Ala Leu Asp Ser Val Ser Gly Leu Glu Gln Gly His
665 670 675

Thr Gln Tyr Leu Ala Ser Ser Glu Asp Ala Ser Ala Leu Val Ala
680 685 690

Ala Leu Thr Arg Phe Ser His Leu Ala Ala Asp Thr Ile Val Asn

695 700 705

Gly Ala Ala Thr Ser His Leu Ala Pro Thr Asp Pro Ala Asp Arg
710 715 720

Leu Met Asp Thr Cys Arg Glu Cys Gly Ala Arg Ala Leu Glu Leu
725 730 735

Val Gly Gln Leu Gln Asp Gln Thr Val Leu Arg Arg Ala Gln Pro
740 745 750

Ser Leu Met Arg Ala Pro Leu Gln Gly Ile Leu Gln Leu Gly Gln
755 760 765

Asp Leu Lys Pro Lys Ser Leu Asp Val Arg Gln Glu Glu Leu Gly
770 775 780

Ala Met Val Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu
785 790 795

Asp Ala Val Arg Arg Ile Glu Asp Met Met Ser Gln Ala Arg His
800 805 810

Glu Ser Ser Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Asn
815 820 825

Ser Cys Thr Asp Leu Met Lys Ala Ile Arg Leu Leu Val Met Thr
830 835 840

Ser Thr Ser Leu Gln Lys Glu Ile Val Glu Ser Gly Arg Gly Ala
845 850 855

Ala Thr Gln Gln Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu
860 865 870

Gly Leu Ile Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Gln
875 888 885

Leu Val Glu Ser Ala Asp Lys Val Val Leu His Met Gly Lys Tyr
890 895 900

Glu Glu Leu Ile Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala
905 910 915

Gln Leu Val Ala Ala Ser Lys Val Lys Ala Asn Lys Asn Ser Pro
920 925 930

His Leu Ser Arg Leu Gln Glu Cys Ser Arg Thr Val Asn Glu Arg
935 940 945

Ala Ala Asn Val Val Ala Ser Thr Lys Ser Gly Gln Glu Gln Ile

950 955 960

Glu Asp Arg Asp Thr Met Asp Phe Ser Gly Leu Ser Leu Ile Lys
965 970 975

Leu Lys Lys Gln Glu Met Glu Thr Gln Val Arg Val Leu Glu Leu
980 985 990

Glu Lys Thr Leu Glu Ala Glu Arg Val Arg Leu Gly Glu Leu Arg
995 1100 1105

Lys Gln His Tyr Val Leu Ala Gly Gly Met Gly Thr Pro Ser Glu
1110 1115 1120

Glu Glu Pro Ser Arg Pro Ser Pro Ala Pro Arg Ser Gly Ala Thr
1125 1130 1135

Lys Lys Pro Pro Leu Ala Gln Lys Pro Ser Ile Ala Pro Arg Thr
1140 1145 1150

Asp Asn Gln Leu Asp Lys Lys Asp Gly Val Tyr Pro Ala Gln Leu
1155 1160 1165

Val Asn Tyr

(2) INFORMATION FOR SEQ ID NO:12:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 12:
GAAGATACCC CACCAAAC 18

(2) INFORMATION FOR SEQ ID NO:13:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other DNA
(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 13:
GCTTGACAGT GTAGTCATAA AGGTGGCTGC AGTCC 35

(2) INFORMATION FOR SEQ ID NO:14:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 14:
GGACATGTCC AGGGAGTTGA ATAC 24

(2) INFORMATION FOR SEQ ID NO:15:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other nucleic acid
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: yes
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 15:
CUACUACUAC UACUAGGCCA CGCGTCGACT AGTACGGGII GGGIIGGGII G 41

(2) INFORMATION FOR SEQ ID NO:16:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 516
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human

(x) FEATURE: exon 1 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 16:

```
TCTGTGGAAG GTTTGGAGGG GAGAGAGGGG CAGCTGGATG CTCTTGGGCC ACGGTCGCCC    60
CTGATCTCTG CGCCTCTTCC TCCTGCTCCG GGAGAAATAA TGTTTCCCTG GGGGATGAAA   120
GCATCTCTTT GTGCGGGCTT TAATTGCCAT GTTGTTGTGC CAAGGGAGTG AGTGGCGGCG   180
GGACCAGCAG CTGGGCACAG CCAATGCCAG GCAGTGGTGC CCACTCCCTC AGGACGCCCA   240
GCCAGCTGGC TCCTGGGAGC GCTGCCCACC TCTGCCCCCA GCTGGGCGCC TGCAAGGAAC   300
CGACCACCCG TGGGGCTGGG GGAGGTTGGC TGGAGGAGGA GAAAGGGGCG GGCTCTGGGA   360
GGGTCTCAGC CACTCTCAGA GGCTTATTCA TCTCATCCTC CTTTCCCTCC CCCTTCTTGT   420
TTTTCAGACT GTCAGCATCA ATAAGGCCAT TAATACGCAG GAAGTGGCTG TAAAGGAAAA   480
ACACGCCAGA AATATCCTTT GGATGTTGCT TGGAAG                              516
```

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 193

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exon 2 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 17:

```
TGTTTTCCAT AACCCCCCCT CACCGTGCAT ACTGGGCACC CACCATGAGA AAGGGGCACA    60
GACCTTCTGG TCTGTTGTCA ACCGCCTGCC TCTGTCTAGC AACCCAGTGC TCTGCTGGAA   120
GTTCTGCCAT GTGTTCCACA AACTCCTCCG AGATGGACAC CCGAACGTGA GTTCCTGGGG   180
CTATGGGGTG GCA                                                      193
```

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 104

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exon 3 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 18:

```
GTGTTCTTTT GCCCCTGCAG GTCCTGAAGG ACTCTCTGAG ATACAGAAAT GAATTGAGTG    60
ACATGAGCAG GATGTGGGTG AGTTTGGAGA TGTACTCAGG AGCC                     104
```

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 327
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 4 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 20:

```
AATTCCTGGC TGCAGATCTC TTGACTGTTA TGTTCTTGTT GTTGACTCTG TTTCCCCTCC   60
TCTTCCTAAA AGGGCCACCT GAGCGAGGGG TATGGCCAGC TGTGCAGCAT CTACCTGAAA  120
CTGCTAAGAA CCAAGATGGA GTACCACACC AAAGTGAGTC TCTGCGGACA GTTCTGCCGC  180
CACCGCCGCC TCCCCTGCTC CATCCCTTCA GCCCCTCCCT GGGCTCATTT GTCAGCTCTT  240
TCAGGTAATA GACAGCCCAG GCTTCTGAGG AAGTGTGCAC ATCATGTACC CAAGCTGTGA  300
GAGAGGAAAG CCACCGCCAG GCCCACG                                       327
```

(2) INFORMATION FOR SEQ ID NO:21:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 331
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 5 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 21:

```
GGGCTCAAGC AATCCTCCCA CCTCGGCCTC CCAAGTAGCT GGGACCACAG GCGTGTGCCA   60
CCACGCCCGG CTGAGAGAGG GCTCTTCATG TCTTCTGCCC TGACTCCCTT CCTCTGCCTC  120
CCTTCCAGAA TCCCAGGTTC CCAGGCAACC TGCAGATGAG TGACCGCCAG CTGGACGAGG  180
CTGGAGAAAG TGACGTGAAC AACTTGTAAG TGGCTCCTGC CCTGAGCCCA GGGAGGGAGA  240
AAGCTTTTGT GAATGCTGAC ACTTCTCATA AGGGTCATGG AGGGCCTGAT GGGGGGAGGC  300
CGTGGCTGGG ATGGGGACCA AAGCCCCTGG G                                  331
```

(2) INFORMATION FOR SEQ ID NO:22:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 470
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 6 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 22:

```
ACTGTCGCTG TCACTGTTGA CTTCACCAGG CTGCATGGCC ATAATACCCA CAAGGCTAAG     60
ACTTGGAGCT GGAGTTGTGT GTGTGTTTGC GCATGCACAT GAGCATTGGA GACTGGAGTA    120
GCGTAGAGCG TGGGGGAGGG GACAGGTAAC AGACCGGCCT CAGGCTGTGG AGTGTAAGCT    180
CTCTTTCCTC TTGGGTCCAG TTTCCAGTTA ACAGTGGAGA TGTTTGACTA CCTGGAGTGT    240
GAACTCAACC TCTTCCAAAC AGGTGAGTCT CTTCCCTCCC GTCTAACCCA GGCTCTCATG    300
GGAACTACCT AATTCCTAGT CCTCCTCTCC CTGCAAAGTG TGCAGCACAA GGGGTAGGAA    360
AATGGAGACA TTCACACCCC ATCTCTGGTC TCTCCAACCC TCGTGCAGGG AGGGACTGAA    420
CCTCTTCAGT ATTTTTCTTT TTAAGAGACA AGGTCTCGGC CGGGTGCAGT               470
```

(2) INFORMATION FOR SEQ ID NO:23:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 565
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 7 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 23:

```
TCTTCACCTG TTTAATGGGG ATACGTTTAC CTATCTCATG GGAGTGTTGT GAAGGTTAAA     60
TGAATTAGAT GAGGTAAAGC ACGCACAGAA TCGGTCCTTG GTGTATGTTG GACCCCTGCC    120
TCTGCCCCTC TGAAGAGGCT GCCTGTAATC CCCTGGCTCT ACCACCTTTC TCCCTCACTT    180
TTATTTCCTA GTATTCAACT CCCTGGACAT GTCCCGCTCT GTGTCCGTGA CGGCAGCAGG    240
GCAGTGCCGC CTCGCCCCGC TGATCCAGGT CATCTTGGAC TGCAGCCACC TTTATGACTA    300
CACTGTCAAG CTTCTCTTCA AACTCCACTC CTGTGAGTAC CGCGGGCCAG ATCTTCTTAC    360
ATGAGATTCA GGCCAGAGGG AGGATCCCAG CCTGAGGATG TCCCCAGAGA AACGCAGTCC    420
TTCTCAGTGC CTTTGGCTGT CTGCTTCTGT TCCAAAAGGC CCCGGAGCTT CTGACCATTG    480
TGAGGATAAA AGAGCAGGGC CCAGGCTTTG GTGACCCCAG TAAAGCCCCT GGCTTGCCAC    540
TCTTGCGTCC AGTGTTACAG GATCT                                          565
```

(2) INFORMATION FOR SEQ ID NO:24:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 233
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 8 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 24:

```
GGGACAGCTC TAGGCCAGTC GTGGCCCCTG GCAGTGCTGG CCACATGCCC CAGGGTAGCT    60
GGGCCCCTCC CCCTCGAGAG CCCCGCTGTG GCTTCCCTGC CCTCTGGTCC CCCTCCCCTC   120
TCACACTCTT TCCAATTTCT TCCAGGCCTC CCAGCTGACA CCCTGCAAGG CCACCGGGAC   180
CGCTTCATGG AGCAGTTTAC AAAGTAAGTG GTTCAAGTAA CAGGAATGGA GGT          233
```

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 578

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exons 9 and 10 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 25:

```
TGAATCCCAG CACCATGGAG TTTATCTCCT TGACAGCCTG TGCCTTTGGG CTGGGGAGGG    60
GGCAGGAAAG CCAGGTGGCT GCTCTGTCCC CTACATGGGG CTGATGAAGA CACCCAGCAC   120
CCCTCAGGTC CTTCTCCACC CCTAGGTTGA AAGATCTGTT CTACCGCTCC AGCAACCTGC   180
AGTACTTCAA GCGGCTCATT CAGATCCCCC AGCTGCCTGA GGTAAGCATG CCCAACCACA   240
CACCCTCGGC ACTGCAGAGG CCCCAGGTAC TCTCTTAAGG GCCGGCGGGG CCTGGCAAGC   300
AAGCACTATT TGAGGATGTG TCTCCGTCTT CAGAACCCAC CCAACTTCCT GCGAGCCTCA   360
GCCCTGTCAG AACATATCAG CCCTGTGGTG GTGATCCCTG CAGAGGCCTC ATCCCCCGAC   420
AGCGAGCCAG TCCTAGAGAA GGATGACCTC ATGGACATGG ATGCCTCTCA GCAGGTGAGG   480
ACCACTTGGG AGAGAAACTT GGCCTTTCCT CTCACCTGCA AGTACAGGGG AGAGGCTGGG   540
GGAGACCCTG GCCAAAGCCC ATTGACTCTA ACCAGGTT                           578
```

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 390

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exon 11 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 26:

```
AAAAAAATTT AAAAAATTAA ACAGGTCTGA ACCGTTTAAT TCGAGAAAGG GGGCATTCTC    60
CCATATCACT CAACTGACCC ACACACAGAA TTCTCTGGCT CTCTGACTTA TTCTCACTCC   120
TTTTTGGTCA ACCACAGAAT TTATTTGACA ACAAGTTTGA TGACATCTTT GGCAGTTCAT   180
TCAGCAGTGA TCCCTTCAAT TTCAACAGTC AAAATGGTGT GAACAAGGAT GAGAAGTGAG   240
TCCAAGCTGG GTTCAAGCAG ATGGTTCAGG AGCTAAGTTA AGCCATGGTC TGCCTCAAAA   300
CACTAACCAA AGAGGAATTC TTAATGATAC TGGGGCTTCT TAGATACAGA ACATCTTGAA   360
GGGTTGGGGG CAATGGCTTA TGCCTGTAAT                                    390
```

(2) INFORMATION FOR SEQ ID NO:27:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 547
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 12 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 27:

```
AAAATCAATA ACCATGGATT TATGAGTATT AGATTAGTAT CTGGTAACAT TTAGAGTATA     60
ATTTATGGCA TTTCAAAGAA TTGTCCCCAA ATTAATACCA GCTTTTAATT TCCTCCCCTG    120
AGCTCACAAT TAAAAACAGA GGGATAGAAG CACTATGAAA GCAAACTCAT TCCCCTTCTC    180
TTCCCAGGGA CCACTTAATT GAGCGACTAT ACAGAGAGAT CAGTGGATTG AAGGCACAGC    240
TAGAAAACAT GAAGACTGAG GTATAACTTG GATCTGCTCT GCCTTTGCGC TTCACCAAAA    300
CACGGTAGAT TTGAATGTTA AATTTGCATC ACACTAGCCA GGCACAGTGG CTCACACCTG    360
TAATCCTAGC ACTTTGGGAG GCCAAGGCAG GAGGATTACC TGAGGTCGGG AGTTCGAGAC    420
CAGCCTGGGC AACAGGGTGA AACCCCCGTC TTCAATAAAA ATGCAATAAT TAGCCGGGTG    480
TGTTGGCAGG CACCTGTAAT CCCAGCTACT CGGGAAGCTG AGGCATGAGA ATTGCTTGAA    540
CTTGGGA                                                              547
```

(2) INFORMATION FOR SEQ ID NO:28:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 436
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 13 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 28:

```
CCCCCAGCCA CTCTAAAGAG GACCACAATT CCCCGGCCAT CATCCCCTGT TATTGTTGTT     60
GATTGAGGGG CTCCTAATGA CCAGATGGTC CAACCCTCCT GGGACGTGGA GAGTTGACTT    120
AGGGGAATCA GGTATTTACT TGGAAGCATG GTAGGACCCG CTTCTCCGGC CCATGCCCGT    180
GACCCGTGGC AGTGGGCGGT TGGCCTCATG ACCGGAGTCC CCCCACAGAG CCAGCGGGTT    240
GTGCTGCAGC TGAAGGGCCA CGTCAGCGAG CTGGAAGCAG ATCTGGCCGA GCAGCAGCAC    300
CTGCGGCAGC AGGCGGCCGA CGACTGTGAA TTCCTGCGGG CAGAACTGGA CGAGCTCAGG    360
AGGCAGCGGG AGGACACCGA GAAGGCTCAG CGGAGCCTGT CTGAGATAGA AAGTGAGCGG    420
TGGGTGGGGG CGGGGG                                                    436
```

(2) INFORMATION FOR SEQ ID NO:29:
(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 469
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 14 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 29:

```
GACTTGAGCC CAAGGAGGTC AAGGCTGCAG TGAACAGTGA TTGTGCCACT GCACCCCAGC      60
CTGGGTGACA GAGCAAGACT GTCTCAAAAC AAAACAAGGA GGACCTTCTA GGGACCCTGG     120
CTCATTGCAA GGAAGGCAAG GGTCCCTGCT AGGTTAGACT CCTCACCTTG GTCCTTTACA     180
ATACAGGGAA AGCTCAAGCC AATGAACAGC GATATAGCAA GCTAAAGGAG AAGTACAGCG     240
AGCTGGTTCA GAACCACGCT GACCTGCTGC GGAAGGTAAG ACCCTCAGCC CCTGTCACCA     300
TCCTGCAGGC CCTGCACCTC TAGGGAGAGA GCGGCTCAGG CCTGTGGCTT CCCCGGGGCC     360
AGCAACCCCT ACATTGATCT CTAAGGCATT GCCGTCATCT CGGGAACCAC ACCTTTTCAG     420
GCTTCCTTGC CTCTGTGTCT TGGGCTGTGT CCTGGGTGCC AATCCCATG                 469
```

(2) INFORMATION FOR SEQ ID NO:30:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 359
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 15 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 30:

```
GGGTAGGAAA GTGATTCCTG TGTCTGACTC TAGGGCACGC ACAGCCTGAG TATGATTGTC      60
CTAGAAGGAG GATGTCCTCT AAGCCTGGGA TCTCCTGGTT CAAGACACTG TTCTTCTTTT     120
GCAGAATGCA GAGGTGACCA AACAGGTGTC CATGGCCAGA CAAGCCCAGG TAGATTTGGA     180
ACGAGAGAAA AAAGAGCTGG AGGATTCGTT GGAGCGCATC AGTGACCAGG GCCAGCGGAA     240
GGTGAGTGGG ACGAGGAGCA CTCGGGAAAT GAGGGAGGGG GCTGTTGAGT TGGTGGCGGG     300
GGCTTTGTGG CCTTCTGCTC CATGGGCAGT TCTGTGGGTC GGTTGGCATC ACACAGCAG      359
```

(2) INFORMATION FOR SEQ ID NO:31:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 209
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 16 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 31:

```
GTTGATCGCT TGGGACGTTT TTACATTTTT ATATTCTTTG TCACTGTCAC CCAGATCAGA      60
GTCCCTCTGT TTTTCTTCTC TTTCAGACTC AAGAACAGCT GGAAGTTCTA GAGAGCTTGA     120
AGCAGGAACT TGCCACAAGC CAACGGGAGC TTCAGGTTCT GCAAGGCAGC CTGGAAACTT     180
CTGCCCAGGT AAATACCTCC TTTTTTTTT                                       209
```

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 485
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 17 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 32:

```
CCCCCACTGC AATCAGTGTG TCCCCGGGAG GGAATCAGAG TGGCAGGTTA AAGAGCCATC      60
ACCTTCCCAG TCCTTGCAAC CCGGTGGTGG GTTGGACCTC TGGGAAGTAG GGACTGTTTA     120
ACTCAACCAG CGTCTCCCTC TTTCCTTGTG GTCACCTTTG CAGTCAGAAG CAAACTGGGC     180
AGCCGAGTTC GCCGAGCTAG AGAAGGAGCG GGACAGCCTG GTGAGTGGCG CAGCTCATAG     240
GGAGGAGGAA TTATCTGCTC TTCGGAAAGA ACTGCAGGAC ACTCAGCTCA AACTGGCCAG     300
CACAGAGGGT CACGGACATG GACACGAGCG AGCACCTGTG AATTCCCACC GAGGGCCTCT     360
GCGCATGCAC GGAGGCTGGG AGGACCCCGG GGCTGCTGAG AAGGGGTTTG GGGCCTTGGC     420
CTGATTGTGC AGACATTCTG TAGGTGTAAT GCCAGCAGGC CCTGCATTGC CTGCAGAGTC     480
CATGA                                                                485
```

(2) INFORMATION FOR SEQ ID NO:33:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 468
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 18 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 33:

```
TTACTGGCTT GGACCTCATT GGCCATGACT TGAGCTAAGA TGCTAAGAGC CCCAGCCAGG      60
TCATCCTGCT CAGGTTCATT ATGGAGTCTA GGGCAGACTC TCACCTCCCT GGACCATTTT     120
```

```
TAGAATCTAT GTGCCAGCTT GCCAAAGACC AACGAAAAAT GCTTCTGGTG GGGTCCAGGA      180
AGGCTGCGGA GCAGGTGATA CAAGACGCCC TGAACCAGCT TGAAGAACCT CCTCTCATCA      240
GCTGCGCTGG GTCTGCAGGT ACACTTGCAA TTGCCCAGCT GGCAGGGGCC AGGTCCTTAC      300
AGCCTGAGAC TCTGTTGATG TTGAATCTCA TGTGAGACTT AGCTCAGGGG CTCTCAGCCC      360
AGCAGCATGT CAGCATTACC TTAGGGGCGC CCAGGCCCCA TCCTAGATCA GTTACATGTG      420
GAAACTCTGT GCATTAGTGC CTATACACTA GTATTTTAGT ATTTTCTT                   468
```

(2) INFORMATION FOR SEQ ID NO:34:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 393
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 19 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 34:

```
CACTAGTAAG CTCCTCCATT CAGTGCTTAA TTAACGAGGA TGAAGCCAGC TATGAGAACT       60
TGCTCTGACC TTGCCCTGTG TTCCCTCTCA CAGATCACCT CCTCTCCACG GTCACATCCA      120
TTTCCAGCTG CATCGAGCAA CTGGAGAAAA GCTGGAGCCA GTATCTGGCC TGCCCAGAAG      180
GTAAGAATGG CCAAGGACAG TCTCTGTCGG CTAGTGATGG CCAGACAGGG TTCAGAAGCA      240
CCTGAATGCG GGGATAGTGA CAGGTCCCTC TGCATCAAGA AAGGCATGTA GGCAACTCAT      300
ACAAGAAAGG CATGTAGGCA ACTCATAAAA CGGGAGGAGA GGGTATGAAA GTGTCACCAT      360
CAACCAGACC TGAGAAACTT CTCTTTCCAA TCC                                   393
```

(2) INFORMATION FOR SEQ ID NO:35:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 421
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 20 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 35:

```
GGCCTGCCCA GAAGGTAAGA ATGGCCAAGG ACAGTCTCTG TCGGCTAGTG ATGGCCAGAC       60
AGGGTTCAGA AGCACCTGAA TGCGGGGATA GTGACAGGTC CCTCTGCATC AAGAAAGGCA      120
TGTAGGCAAC TCATACAAGA AAGGCATGTA GGCAACTCAT AAAACGGGAG GAGAGGGTAT      180
GAAAAGTGTCA CCATCAACCA GACCTGAGAA ACTTCTCTTT CCAATCCTGG CAGACATCAG     240
TGGACTTCTC CATTCCATAA CCCTGCTGGC CCACTTGACC AGCGACGCCA TTGCTCATGG      300
TGCCACCACC TGCCTCAGAG CCCCACCTGA GCCTGCCGAC TGTGAGTACT GGGGCATGAG      360
GGGCTGTTCA TGGACCAGGG GAGCAGGGGG CCTTTAAAAG TCTCTGTTGG GCCGGGCGCA      420
G                                                                      421
```

(2) INFORMATION FOR SEQ ID NO:36:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 498
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 21 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 36:

```
AGGCCGAGGC AGGAGAATCG CTTGAACTCA GGAGGCGGAG TTTGCAGTGA GCCGAGATGG      60
CGCCACTGCA CTCCAGCCTG GGCAACAAGA GCGAGACTCC ATCTCAAAAA AAAAGTGTCT     120
ATTGCCTTGT ATCTCCAGCA CTGACCGAGG CCTGTAAGCA GTATGGCAGG GAAACCCTCG     180
CCTACCTGGC CTCCCTGGAG GAAGAGGGAA GCCTTGAGAA TGCCGACAGC ACAGCCATGA     240
GGAACTGCCT GAGCAAGATC AAGGCCATCG GCGAGGTACT TGGAGTAGTA TCATTGAGGA     300
GCATTGTTAT TCTTCTGGGT GTGCGTGCTG GTGAATGGCC AGGGAATCGG TGATGTTCTG     360
AGCTAGTTCT TTCTGCACTT AGAACTTGAT TCTAGAAAGA GATTGTTAAA ATTGGAAAAT     420
CTGGCCGGGT GCAGTGATTT ATGCGTGTAA TCCCAGCACT TTGGGAGGCC GAGTCAGGAG     480
GATCACTTGA GGCTAGAC                                                   498
```

(2) INFORMATION FOR SEQ ID NO:37:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 427
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 22 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 37:

```
CCCTGTGGCT TGCAGAAGGT GTTTGCTGGG TGGCCTCCTG CCTTGCCATC TTGTAAGGGT      60
TACAGATGGC AGAGGAGAAG AGACAGGAGG CCCCAAGGTC AGTTCAGCCT TTGTGATGTG     120
TTCACAGGAG CTCCTGCCCA GGGGACTGGA CATCAAGCAG GAGGAGCTGG GGGACCTGGT     180
GGACAAGGAG ATGGCGGCCA CTTCAGCTGC TATTGAAACT GCCACGGCCA GAATAGAGGT     240
AGGAGGTTCC TGCAGGATCT CCTGAAACGA TGCCTTTGCA GCTGCCCTTC TGCAACACTG     300
CTCATTAAAC ATGTCACAGT CGTTCATTAA GGCCATGGCA ACCCCCTAAG ACAGAAACCA     360
GAATTTGCCA GGCACAGTGG CTCATGCCTG TAACCCCAGC ACCTTGGGAG GATCACTTGA     420
GTCCAGG                                                               427
```

(2) INFORMATION FOR SEQ ID NO:38:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 367

(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 23 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 38:

```
CCCCCTGAAT AGGTTAGAGT CTGGATTCTT TTCTGACTCT CTCAAGAATG TGGGCAGGGA      60
CTTGGGGACT TCCAGATTCA GGTTTCCCAG CTACCACACG ATGTTGGACT GAAAGTATAG     120
TAAGACATTA GTGGATCCTT AATATTCAAG GCACATTTAG AAACCATGCT TCTTTTTCAC     180
AGGAGATGCT CAGCAAATCC CGAGCAGGAG ACACAGGAGT CAAATTGGAG GTGAATGAAA     240
GGTCGGTCTG AGCGGCATGG TGGGACCTAG GGGAGCAGGA TCTGTCTTCC TGACATTGGT     300
CTATACTTTG CATACTTATT AGGGAATTAG AGGAGAGCAG TAGCAGCCAC GGGGAAGGGC     360
TGAGTTG                                                               367
```

(2) INFORMATION FOR SEQ ID NO:39:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 502
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 24 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 39:

```
CCCCGCAGAA TGTTCCAGCA ACCTCAGCAC CCTTCTTACC TCCCTTTCCC ATTCCAAGCT      60
TGCCTTTGGC TAGGAGTGGG GAAGAGAACC GTCGTGTTCA TTGATCTTGG ATCTTGATCT     120
CAGTGTATCC TCGACTTGTT TGTTTGGCAG GATCCTTGGT TGCTGTACCA GCCTCATGCA     180
AGCTATTCAG GTGCTCATCG TGGCCTCTAA GGACCTCCAG AGAGAGATTG TGGAGAGCGG     240
CAGGGTGAGC GTGGGTGTGG GCCCTGGGCA GGAAGAGGAG GCATCGGTGA CAGACTCCCG     300
CTCCAACGGA CTCTGTGATG CTGCCGTCTT ACTCTGTGTG TCCACCTGAG TACAGAGCAG     360
CCACTCCTGT AGATATCAGC AGAGGCCCTG GGGAGAAGTC AGAGCTCCAG GACCTCCCCA     420
GAGGGTGGCC AGGCATGTGT CCCAACTCCA GCTCCCTTCG CACAGGCAGA CATTGTTGGA     480
ACTTGCTGTG GGAGCCCTTT TT                                               502
```

(2) INFORMATION FOR SEQ ID NO:40:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 437
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 25 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 40:

```
TTTTGGTCTC TGAATCTTCT TCTTTTTTGT AAAATGGGAA TACTAATGCT TATGTCTCAG      60
AGTTACTATG AGGATGATTT GGGATAATAT ATGTATAAAA GCACCTGCCA TATAGTACAT     120
GCTCAATAAA AGGTGGCTAT TACTATTTTT TATTTCCCTA GGGTACAGCA TCCCCTAAAG     180
AGTTTTATGC CAAGAACTCT CGATGGACAG AAGGACTTAT CTCAGCCTCC AAGGCTGTGG     240
GCTGGGGAGC CACTGTCATG GTGTAAGTAT CTATTGGTAC CAAGGGTCCT CCCATGACCC     300
CTCTTCCATT GATCCACTCC AAACAATAGC TAAGGAGGGA AAAAAAAATC TGTCCCTTAG     360
AAATAAACTA TTGATCAGGA AGTCAATAGG ACCGAGTTTA CAAGGGAGCC TGGCTCTCCC     420
AGGGGACACA GGGCAGG                                                    437
```

(2) INFORMATION FOR SEQ ID NO:41:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 351
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 26 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 41:

```
GGGAGCCTGG CTCTCCCAGG GGACACAGGG CAGGCAGCCT CCCCTCCCTG TTTAGCCAAG      60
GGCGATGGGG TGGTCTGGAG GTGGGATTGT GGAGGAGTTG CAGCTCATTT GCCCGTAACC     120
TAGTCCCTCT TGTCGTTTTC CATCAGGGAT GCAGCTGATC TGGTGGTACA AGGCAGAGGG     180
AAATTTGAGG AGCTAATGGT GTGTTCTCAT GAAATTGCTG CTAGCACAGC CCAGCTTGTG     240
GCTGCATCCA AGGTAGGACC TGGCTGGACC TCCTAGGACG CTGGAAGGCC TGGTTAGAGA     300
GTACTAGGCT AGGTTAAAGA GTACTTGGCT GCGTTAGGCA GTACTTGGCT G               351
```

(2) INFORMATION FOR SEQ ID NO:42:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 418
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 27 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 42:

```
CTTTTTATAT GATAGATATG TCAGGAGCTG ACTATAGTCA GCAGATTTTG AGAAGCTGAT      60
TGGTGATTGC CGTTTGGCCC ACATATGTTT GCTAAGAACC ATCAGAGCAA TTATCTGATT     120
CAGTCCTTGT TGCTCTAGGT GTTGTATGAA CCTAAATCTG CTTTGTCCTG GTAGGTGAAA     180
```

```
GCTGATAAGG ACAGCCCCAA CCTAGCCCAG CTGCAGCAGG CCTCTCGGGG AGTGAACCAG      240
GCCACTGCCG GCGTTGTGGC CTCAACCATT TCCGGCAAAT CACAGATCGA AGAGACAGGT      300
AGCCTTTCCA AAGGGACCCT TTTCTTACCC ACCCTGTTGA GCTCTTCTCT GCATCCTTCC      360
CTGTGATCCC AACCAAATCC CACAGGACTG TGTCTAAATT CTTTCATATT TTTCATCT         418
```

(2) INFORMATION FOR SEQ ID NO:43:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 279
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 28 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 43:

```
TTTCCACAGA GCATTGGCAT TGGCTGCCTC TCAGGTGCCA GTCAGCCAGG GTAGAATTTG       60
ATGAGACCTT CTTGTTTCCA TCCTTGCAGA CAACATGGAC TTCTCAAGCA TGACGCTGAC      120
ACAGATCAAA CGCCAAGAGA TGGATTCTCA GGTTAGGGTG CTAGAGCTAG AAAATGAATT      180
GCAGAAGGAG CGTCAAAAAC TGGGAGAGCT TCGGAAAAAG CACTACGAGC TTGCTGGTGT      240
TGCTGAGGGC TGGGAAGAAG GTAAGCTGAC TCAAAGGAT                              279
```

(2) INFORMATION FOR SEQ ID NO:44:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3715
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 29 and partial cds of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 44:

```
AACATAAATT ATCATTGTCT TTTAGGAACA GAGGCATCTC CACCTACACT GCAAGAAGTG       60
GTAACCGAAA AAGAATAGAG CCAAACCAAC ACCCCATATG TCAGTGTAAA TCCTTGTTAC      120
CTATCTCGTG TGTGTTATTT CCCCAGCCAC AGGCCAAATC CTTGGAGTCC CAGGGGCAGC      180
CACACCACTG CCATTACCCA GTGCCGAGGA CATGCATGAC ACTTCCCAAA GACTCCCTCC      240
ATAGCGACAC CCTTTCTGTT TGGACCCATG GTCATCTCTG TTCTTTTCCC GCCTCCCTAG      300
TTAGCATCCA GGCTGGCCAG TGCTGCCCAT GAGCAAGCCT AGGTACGAAG AGGGGTGGTG      360
GGGGGCAGGG CCACTCAACA GAGAGGACCA ACATCCAGTC CTGCTGACTA TTTGACCCCC      420
ACAACAATGG GTATCCTTAA TAGAGGAGCT GCTTGTTGTT TGTTGACAGC TTGGAAAGGG      480
AAGATCTTAT GCCTTTTCTT TTCTGTTTTC TTCTCAGTCT TTTCAGTTTC ATCATTTGCA      540
CAAACTTGTG AGCATCAGAG GGCTGATGGA TTCCAAACCA GGACACTACC CTGAGATCTG      600
CACAGTCAGA AGGACGGCAG GAGTGTCCTG GCTGTGAATG CCAAAGCCAT TCTCCCCCTC      660
TTTGGGCAGT GCCATGGATT TCCACTGCTT CTTATGGTGG TTGGTTGGGT TTTTTGGTTT      720
TGTTTTTTTT TTTTAAGTTT CACTCACATA GCCAACTCTC CCAAAGGGCA CACCCCTGGG      780
GCTGAGTCTC CAGGGCCCCC CAACTGTGGT AGCTCCAGCG ATGGTGCTGC CCAGGCCTCT      840
```

```
CGGTGCTCCA TCTCCGCCTC CACACTGACC AAGTGCTGGC CCACCCAGTC CATGCTCCAG      900
GGTCAGGCGG AGCTGCTGAG TGACAGCTTT CCTCAAAAAG CAGAAGGAGA GTGAGTGCCT      960
TTCCCTCCTA AAGCTGAATC CCGGCGGAAA GCCTCTGTCC GCCTTTACAA GGGAGAAGAC     1020
AACAGAAAGA GGGACAAGAG GGTTCACACA GCCCAGTTCC CGTGACGAGG CTCAAAAACT     1080
TGATCACATG CTTGAATGGA GCTGGTGAGA TCAACAACAC TACTTCCCTG CCGGAATGAA     1140
CTGTCCGTGA ATGGTCTCTG TCAAGCGGGC CGTCTCCCTT GGCCCAGAGA CGGAGTGTGG     1200
GAGTGATTCC CAACTCCTTT CTGCAGACGT CTGCCTTGGC ATCCTCTTGA ATAGGAAGAT     1260
CGTTCCACTT TCTACGCAAT TGACAAACCC GGAAGATCAG ATGCAATTGC TCCCATCAGG     1320
GAAGAACCCT ATACTTGGTT TGCTACCCTT AGTATTTATT ACTAACCTCC CTTAAGCAGC     1380
AACAGCCTAC AAAGAGATGC TTGGAGCAAT CAGAACTTCA GGTGTGACTC TAGCAAAGCT     1440
CATCTTTCTG CCCGGCTACA TCAGCCTTCA AGAATCAGAA GAAAGCCAAG GTGCTGGACT     1500
GTTACTGACT TGGATCCCAA AGCAAGGAGA TCATTTGGAG CTCTTGGGTC AGAGAAAATG     1560
AGAAAGGACA GAGCCAGCGG CTCCAACTCC TTTCAGCCAC ATGCCCCAGG CTCTCGCTGC     1620
CCTGTGGACA GGATGAGGAC AGAGGGCACA TGAACAGCTT GCCAGGGATG GGCAGCCCAA     1680
CAGCACTTTT CCTCTTCTAG ATGGACCCCA GCATTTAAGT GACCTTCTGA TCTTGGGAAA     1740
ACAGCGTCTT CCTTCTTTAT CTATAGCAAC TCATTGGTGG TAGCCATCAA GCACTTCCCA     1800
GGATCTGCTC CAACAGAATA TTGCTAGGTT TTGCTACATG ACGGGTTGTG AGACTTCTGT     1860
TTGATCACTG TGAACCAACC CCCATCTCCC TAGCCCACCC CCCTCCCCAA CTCCCTCTCT     1920
GTGCATTTTC TAAGTGGGAC ATTCAAAAAA CTCTCTCCCA GGACCTCGGA TGACCATACT     1980
CAGACGTGTG ACCTCCATAC TGGGTTAAGG AAGTATCAGC ACTAGAAATT GGGCAGTCTT     2040
AATGTTGAAT GCTGCTTTCT GCTTAGTATT TTTTTGATTC AAGGCTCAGA AGGAATGGTG     2100
CGTGGCTTCC CTGTCCCAGT TGTGGCAACT AAACCAATCG GTGTGTTCTT GATGCGGGTC     2160
AACATTTCCA AAAGTGGCTA GTCCTCACTT CTAGATCTCA GCCATTCTAA CTCATATGTT     2220
CCCAATTACC AAGGGGTGGC CGGGCACAGT GGCTCACGCC TGTAATCCCA GCACTTTGAG     2280
AGGCTGAGGT GGTAGGATCA CCTGAGGTCA GGAGTTCAAG ACCAGCCTGT CCAACATGGT     2340
GAAACCCCCA TCTCTACTAA AAATACCAAA AATTAGCCGA GCGTAGTGAC GGGTGCCCGT     2400
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(+/- 274.14)
499.6
(+/- 212.39)
356.8
(+/- 56.33)
118.4
(+/- 25.0)
35.0
(+/- 11.0)
12.9
11.0
Activity (Miller Units)
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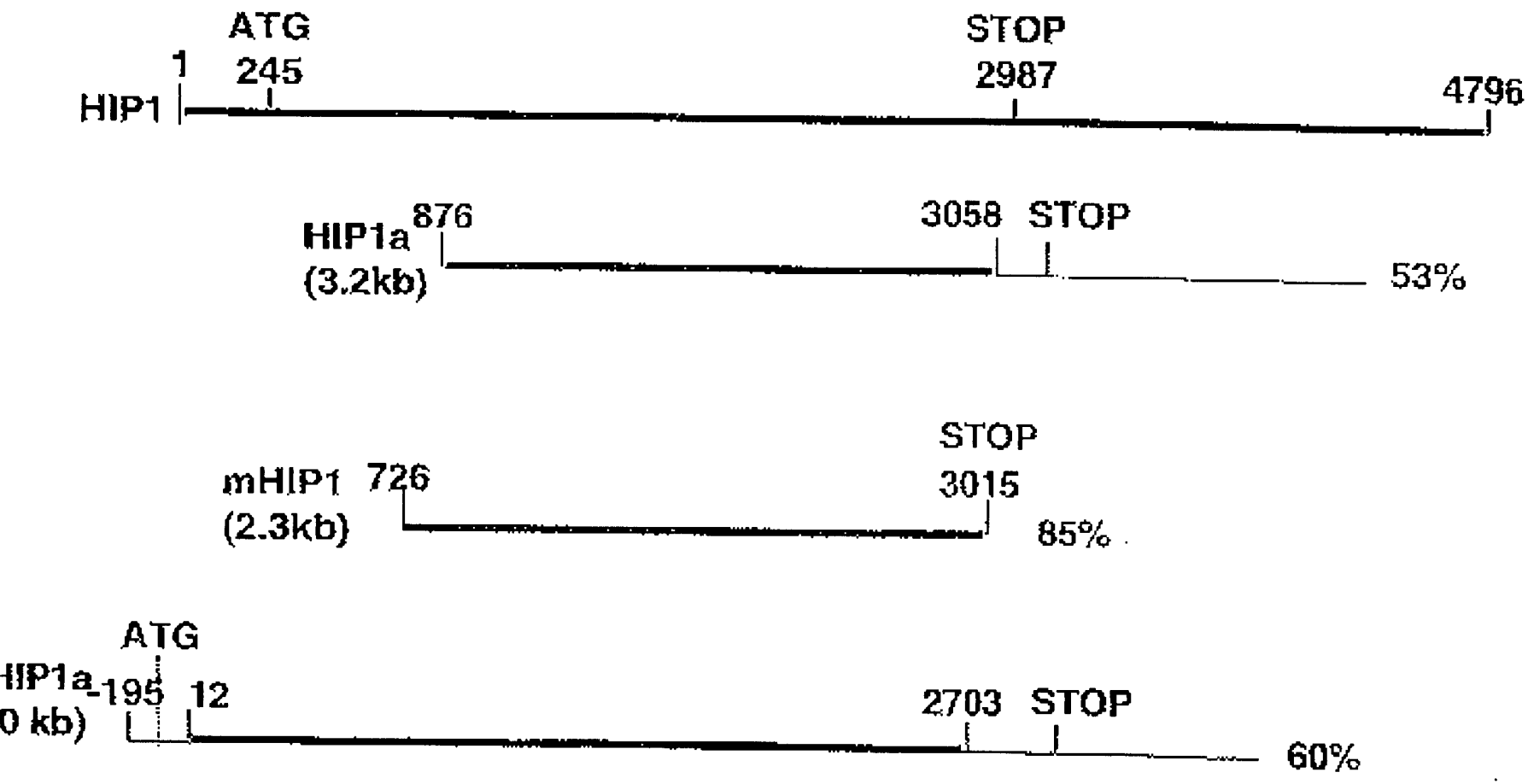
700
600
500
400
300
200
100
0
16pGBT9
44pGBT9
80pGBT9
128pGBT9
DnKpGBT9
pGBT9
Clone+HIP1

Fig. 1

Fig 2

HIP1 Clones: Nucleotide Alignment



WO 99/49986
PCT/US99/01743

Fig 3

HIP1 Clones: Protein Alignment

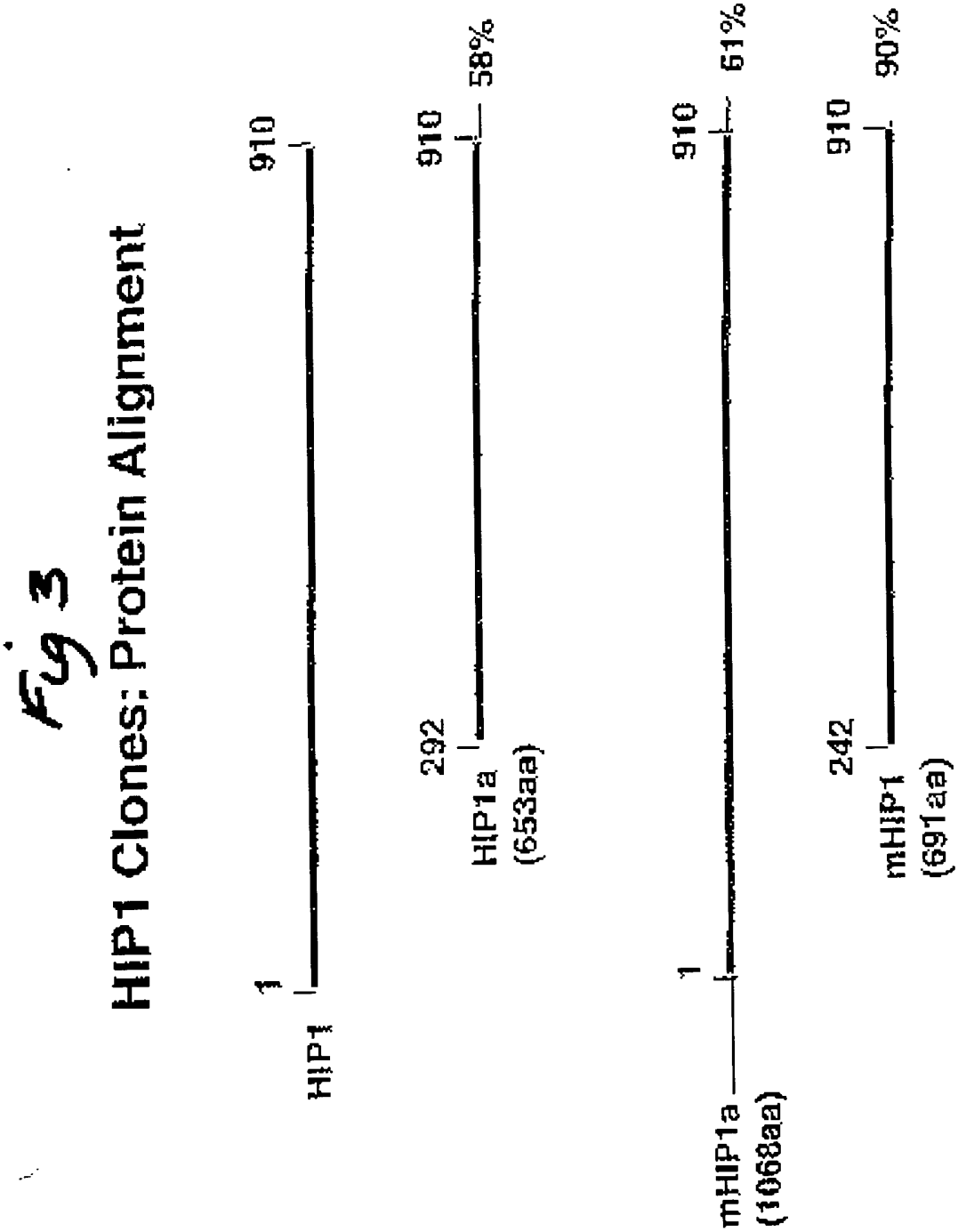


Fig 4

>Usurpin A
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>Usurpin B
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>Casp-8 A
FSRNLYDIGEQLDSEDLASLKFLSLDYIPQRKQEPIKDALMLFQRLQEKRMLEESNLSFLKELLFRINRLDLLITYLN

>Casp-8 B
YRVMLYQISEEVSRSELRSFKFLLQEEISKCKLDDDMNLLDIFIEMEKRVILGEGKLDILKRVCAQINKSLLKIIND

>Casp-10 A
FREKLLIIDSNLGVQDVENLKFLCIGLVPNKKLEKSSSASDVFEHLLAEDLLSEEDPFFLAELLYIIRQKKLLQHLNC

>Casp-10 B
FRNLLYELSEGIDSENLKDMIFLLKDSLPKTEMTSLSFLAFLEKQGKIDEDNLTCLEDLCKTVVPKLLRNIEK

>FADD
FLVLLHSVSSSLSSSELTELKFLCLGRVGKRKLERVQSGLDLFSMLLEQNDLEPGHTELLRELLASLRRHDLLRRVDD

>MC159 A
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>MC159 B
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>E8
FRCLMALVNDFLSDKEVEEMYFLCAPALESHLEPGSKKSFLRLASLLEDLELLSGDKLTFLRHLLTTIGRADLVKNLQV

>K3 orfk13A
TYEVLCEVARKLGTDDREVVLFLLNVFIPQPTLAQLIGALRALKEEGRLTFPLLAECLFRAGRRDLLRDLLH

>K3 orfk13B
YQLTVLHVDGELCARDIRSLIFLSKDTIGSRSTPQTFLHWVYCMENLDLLGPTDVDALMSMLRSLSRVDLQRQVQT

>HIP1
SELEADLAEQQHLRQQAADDCEFLRAELDELRRQREDTEKAQRSLSEIERKAQANEQRYSKLKEKYSELVQNHADLLRKN
AE

>HIP1a
GELSPQRKQKDKALVDNEQLRHELAQLRAAQLEREHSQGLREEAERKASATEARYNKLKEKHSELVHVHAELLRKNAD

>mHIP1a
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>mHIP1
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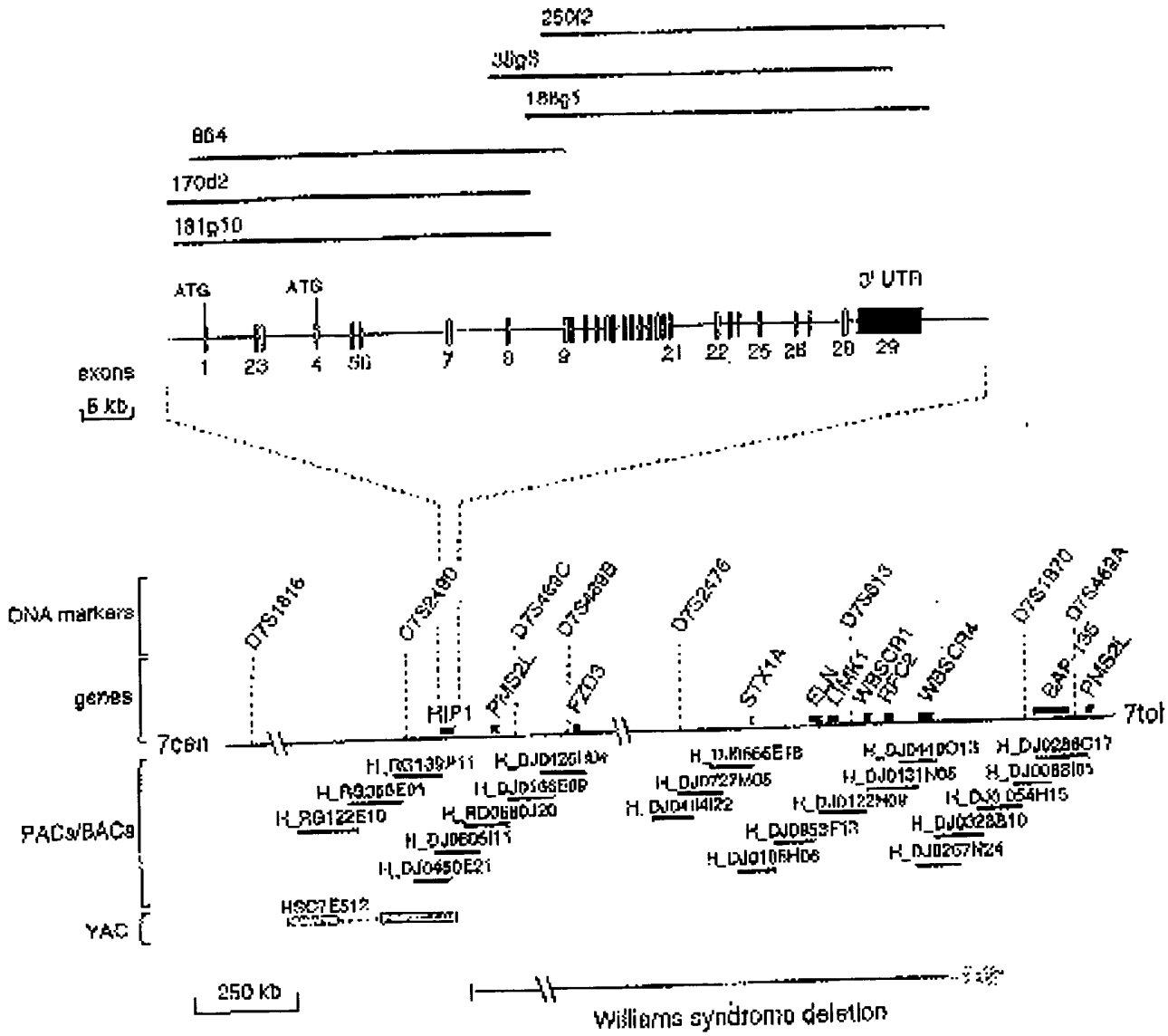
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5 kb
DNA markers
genes
PACs/BACs
YAC
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RIP1
FZD3
STX1A
ELN
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7tel
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Williams syndrome deletion
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Fig 5

Fig 6

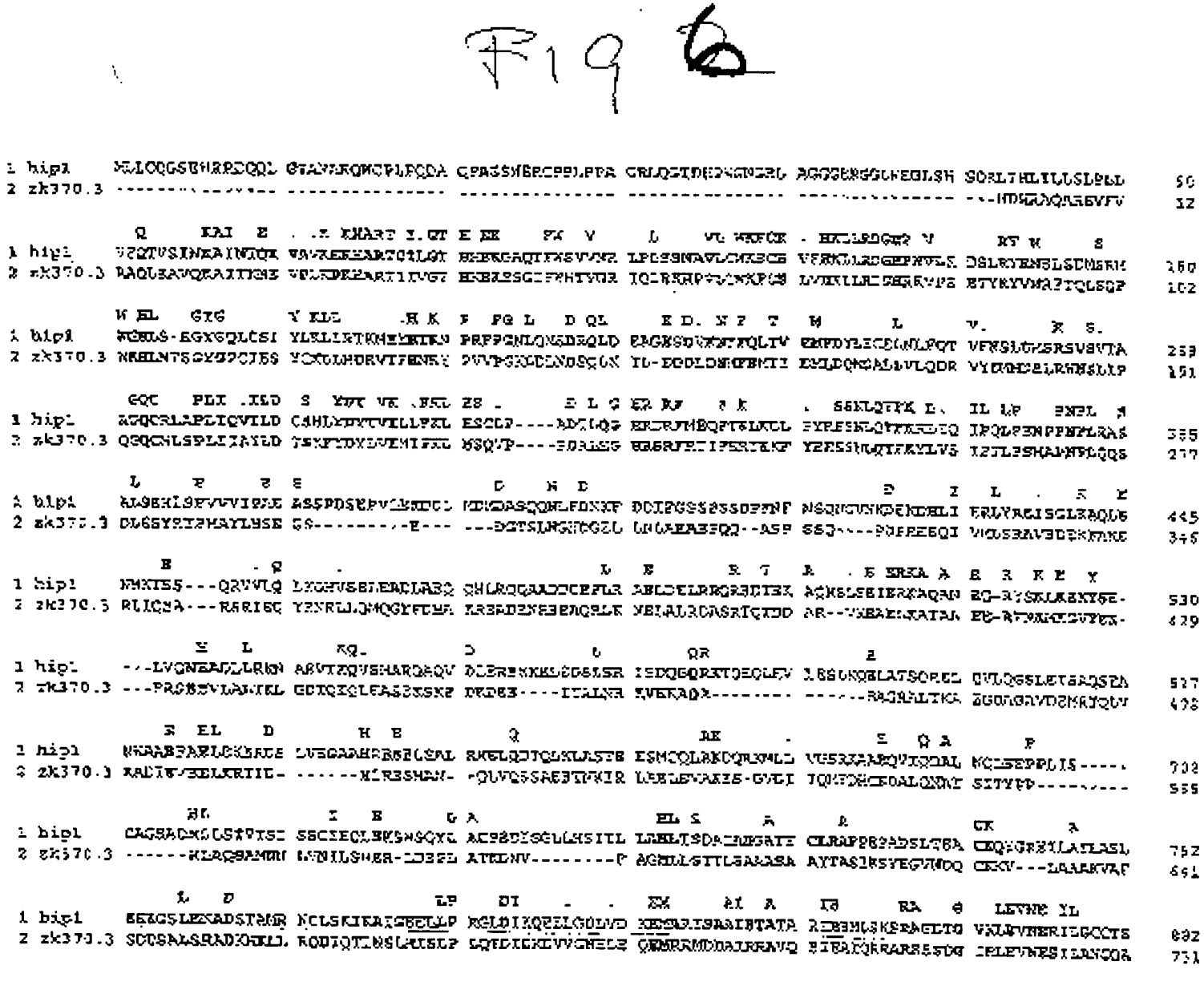

FIG 6 (CONT.)

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2 zk370.3    LMSVIPQLVIASREL QIEIVAAGKAGGGPA NPKSEKNQWIEGLLS AAKAVGVAARVLVES ADGVVIGKGK----V EELIVAAQEIAASTA     517

             QL . E VEADEDSS  L  L  A   VMQ  TD VVA    Q   .           DES   L     K  EK SQV  I ELE  L  ER EL
1 hip1       QLVAASKVKADKDSP NLAQLQQASRGVNQA TAGVVASTISGKSQI EETDN--MDFSSMTL TQIKRQEMDSQVRVL ELENELQKERQKLGE     1036
2 zk370.3    QLIVSSRVKADKDSS KLDALSVAAKAVNQT TAQVVAAVKAGQTTL NDESS--LDFSYLSL HAAKKEMDSQVRSL ELEQELMQEAAKLAA     505

             LRK VY  A .
1 hip1       LRRKHYELAGVASGK EEGTEASPPTLQEVV TEKE     1090
2 zk370.3    LRRQHYHMAQLVAKK VSP------------ ----      523
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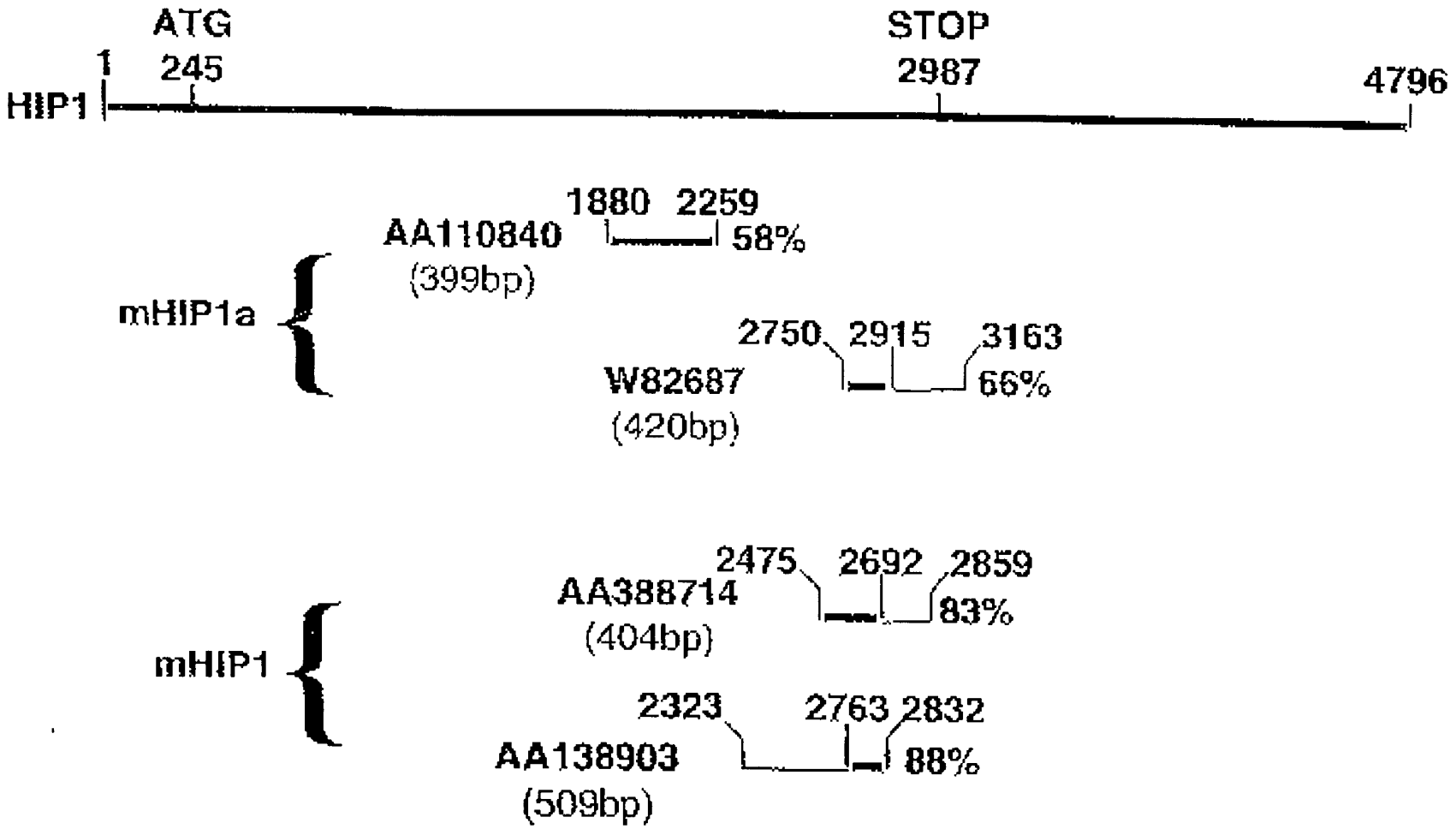
Fig 7

Mouse ESTs



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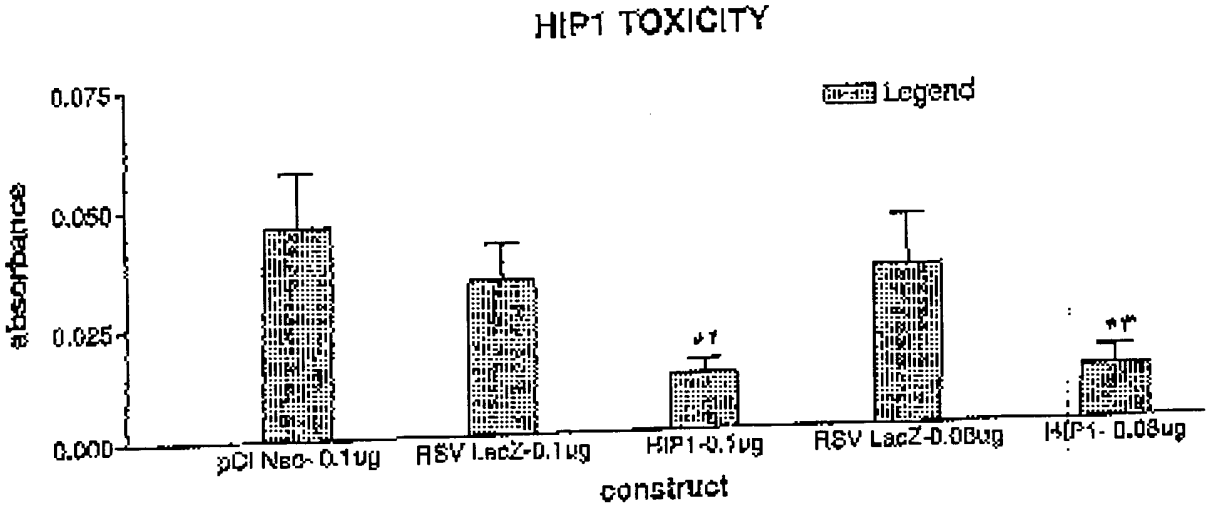

Fig 8

Hip-1 is toxic in the presence of huntingtin

HIP1 transfected into HD1955-15 stable cell line
36 hr post-tansfection

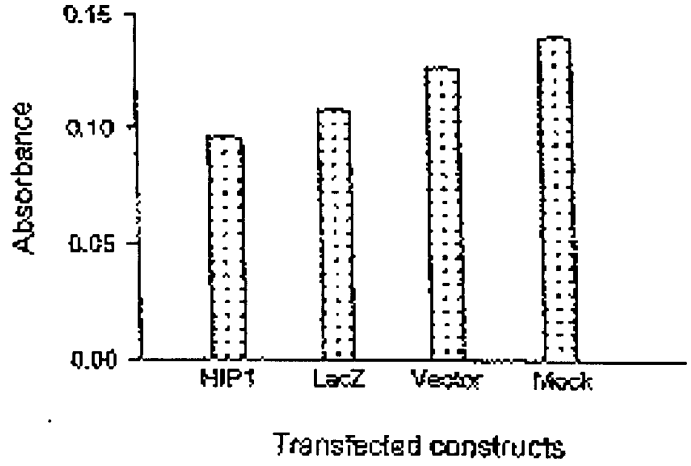

Fig 9A

Hip-1 is toxic in the presence of huntingtin

HIP1 transfected into HD1955-128 stable cell line
36 hr post-tansfection

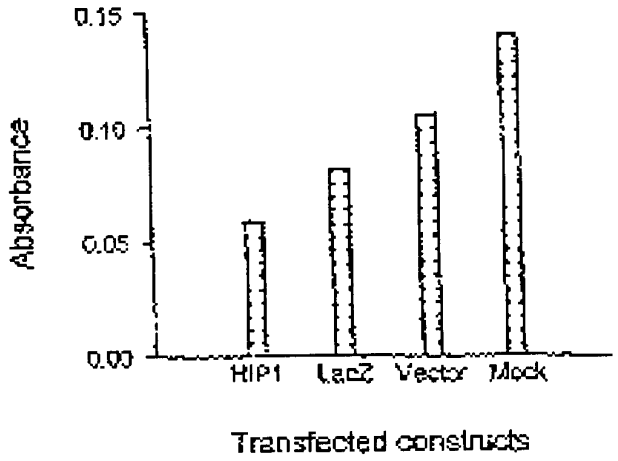

Fig 9B

Polyglutamine-dependence of HIP-1 toxicity

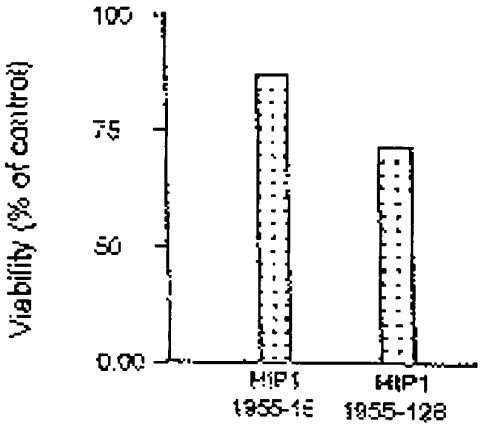

Fig 9C

SEQUENCE LISTING

(1) GENERAL INFORMATION:
(i) APPLICANT:Kalchman, Michael
Hayden, Michael R.
Hackam, Abigail
Chopra, Vikramjit Singh
Nicholson, Donald W.
Vallaincourt, John P.
Rasper, Dita M.
(ii) TITLE OF INVENTION: Apoptosis Modulators That Interact with the Huntington's Disease Gene
(iii) NUMBER OF SEQUENCES: 44
(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Oppedahl & Larson
(B) STREET: PO Box 5270
(C) CITY: Frisco
(D) STATE: CO
(E) COUNTRY: USA
(F) ZIP: 80443-5270
(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette, 3.50 inch, 1.44 Kb storage
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: MS DOS 5.0
(D) SOFTWARE: WordPerfect
(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:
(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Larson, Marina T.
(B) REGISTRATION NUMBER: 32038
(C) REFERENCE/DOCKET NUMBER: UBC.P-013US2
(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (970) 668-2050
(B) TELEFAX: (970) 668-2052

(2) INFORMATION FOR SEQ ID NO:1:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1164
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
(xi)SEQUENCE DESCRIPTION: SEQ ID NO:1:

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(B) TYPE: protein
(D) TOPOLOGY: linear
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(iii) HYPOTHETICAL: no
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(A) ORGANISM: human
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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
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TTCTTCTCAG TCTTTTCAGT TTCATCATTT GCACAAACTT GTGAGCATCA  3550
GAGGGCTGAT CGATTCCAAA CCAGGACACT ACCCTGAGAT CTGCACAGTC  3600
AGAAGGACGG CAGGACTCTC CTGGCTGTGA ATGCCAAAGC CATTCTCCCC  3650
CTCTTTGGGC AGTGCCATGG ATTTCCACTG CTTCTTATGG TGGTTGGTTG  3700
GGTTTTTTGG TTTTGTTTTT TTTTTTAAG TTTCACTCAC ATAGCCAACT  3750
CTCCCAAAGG GCACACCCCT GGGGCTGAGT CTCCAGGCCC CCCCAACTGT  3800
GGTAGCTCCA GCGATGGTGC TGCCCAGCCC TCTCGGTGCT CCATCTCCGC  3850
CTCCACACTG ACCAAGTGCT GGCCCACCCA GTCCATGCTC CAGGGTCAGG  3900
CGGAGCTGCT GAGTGACAGC TTTCCTCAAA AAGCAGAAGG AGAGTGAGTG  3950
CCTTTCCCTC CTAAAGCTGA ATCCCGGCGG AAAGCCTCTG TCCGCCTTTA  4000
CAAGGGAGAA GACAACAGAA AGAGGGACAA GAGGGTTCAC ACAGCCCAGT  4050
TCCCGTGACG AGGCTCAAAA ACTTGATCAC ATGCTTGAAT GGACCTGCTG  4100
AGATCAACAA CACTACTTCC CTGCCGGAAT GAACTGTCCC TCAATGCTCT  4150
CTGTCAAGCG GGCCGTCTCC CTTGCCCCAC AGACGGAGTG TGGGAGTGAT  4200
TCCCAACTCC TTTCTGCAGA CGTCTGCCTT GGCATCCTCT TGAATAGGAA  4250
GATCGTTCCA CTTTCTACGC AATTGACAAA CCCGGAAGAT CAGATGCAAT  4300
TGCTCCCATC AGGGAAGAAC CCTATACTTG GTTTGCTACC CTTAGTATTT  4350
ATTACTAACC TCCCTTAAGC AGCAACAGCC TACAAAGAGA TGCTTCGACC  4400
AATCAGAACT TCAGGTGTGA CTCTAGCAAA GCTCATCTTT CTGCCCCGCT  4450
ACATCAGCCT TCAAGAATCA GAAGAAAGCC AAGGTGCTCG ACTGTTACTG  4500
ACTTGGATCC CAAAGCAAGG AGATCATTTG GAGCTCTTCG CTCAGAGAAA  4550
ATGAGAAAGC ACAGAGCCAG CGCCTCCAAC TCCTTTCAGC CACATGCCCC  4600
AGGCTCTCGC TGCCCTGTGG ACAGGATGAG GACAGAGGGC ACATGAACAG  4650
CTTGCCAGGG ATGGGCAGCC CAACAGCACT TTTCCTCTTC TAGATGGACC  4700
CCAGCATTTA AGTGACCTTC TGATCTTGGG AAAACAGCGT CTTCCTTCTT  4750
TATCTATAGC AACTCATTGG TGGTAGCCAT CAAGCACTTC GGAATT      4796
```

(2) INFORMATION FOR SEQ ID NO: 4:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 924
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

```
Met Ser Arg Met Trp Gly His Leu Ser Glu Gly Tyr Gly Gln Leu
 1               5                  10                  15

Cys Ser Ile Tyr Leu Lys Leu Leu Arg Thr Lys Met Glu Tyr His
            20                  25                  30
```

Thr Lys Asn Pro Arg Phe Pro Gly Asn Leu Gln Met Ser Asp Arg
35 40 45

Gln Leu Asp Glu Ala Gly Glu Ser Asp Val Asn Asn Phe Phe Gln
50 55 60

Leu Thr Val Glu Met Phe Asp Tyr Leu Glu Cys Glu Leu Asn Leu
65 70 75

Phe Gln Thr Val Phe Asn Ser Leu Asp Met Ser Arg Ser Val Ser
80 85 90

Val Thr Ala Ala Gly Gln Cys Arg Leu Ala Pro Leu Ile Gln Val
95 100 105

Ile Leu Asp Cys Ser His Leu Tyr Asp Tyr Thr Val Lys Leu Leu
110 115 120

Phe Lys Leu His Ser Cys Leu Pro Ala Asp Thr Leu Gln Gly His
125 130 135

Arg Asp Arg Phe Met Glu Gln Phe Thr Lys Leu Lys Asp Leu Phe
140 145 150

Tyr Arg Ser Ser Asn Leu Gln Tyr Phe Lys Arg Leu Ile Gln Ile
155 160 165

Pro Gln Leu Pro Glu Asn Pro Pro Asn Phe Leu Arg Ala Ser Ala
170 175 180

Leu Ser Glu His Ile Ser Pro Val Val Val Ile Pro Ala Glu Ala
185 190 195

Ser Ser Pro Asp Ser Glu Pro Val Leu Glu Lys Asp Asp Leu Met
200 205 210

Asp Met Asp Ala Ser Gln Gln Asn Leu Phe Asp Asn Lys Phe Asp
215 220 225

Asp Ile Phe Gly Ser Ser Phe Ser Ser Asp Pro Phe Asn Phe Asn
230 235 240

Ser Gln Asn Gly Val Asn Lys Asp Glu Lys Asp His Leu Ile Glu
245 250 255

Arg Leu Tyr Arg Glu Ile Ser Gly Leu Lys Ala Gln Leu Glu Asn
260 265 270

Met Lys Thr Glu Ser Gln Arg Val Val Leu Gln Leu Lys Gly His
275 280 285

Val Ser Glu Leu Glu Ala Asp Leu Ala Glu Gln Gln His Leu Arg
290 295 300

Gln Gln Ala Ala Asp Asp Cys Glu Phe Leu Arg Ala Glu Leu Asp
305 310 315

Glu Leu Arg Arg Gln Arg Glu Asp Thr Glu Lys Ala Gln Arg Ser
320 325 330

Leu Ser Glu Ile Glu Arg Lys Ala Gln Ala Asn Glu Gln Arg Tyr
335 340 345

Ser Lys Leu Lys Glu Lys Tyr Ser Glu Leu Val Gln Asn His Ala
350 355 360

Asp Leu Leu Arg Lys Asn Ala Glu Val Thr Lys Gln Val Ser Met
365 370 375

Ala Arg Gln Ala Gln Val Asp Leu Glu Arg Glu Lys Lys Glu Leu
380 385 390

Glu Asp Ser Leu Glu Arg Ile Ser Asp Gln Gly Gln Arg Lys Thr
395 400 405

Gln Glu Gln Leu Glu Val Leu Glu Ser Leu Lys Gln Glu Leu Gly
410 415 420

Thr Ser Gln Arg Glu Leu Gln Val Leu Gln Gly Ser Leu Glu Thr
425 430 435

Ser Ala Gln Ser Glu Ala Asn Trp Ala Ala Glu Phe Ala Glu Leu
440 445 450

Glu Lys Glu Arg Asp Ser Leu Val Ser Gly Ala Ala His Arg Glu
455 460 465

Glu Glu Leu Ser Ala Leu Arg Lys Glu Leu Gln Asp Thr Gln Leu
470 475 480

Lys Leu Ala Ser Thr Glu Glu Ser Met Cys Gln Leu Ala Lys Asp
485 490 495

Gln Arg Lys Met Leu Leu Val Gly Ser Arg Lys Ala Ala Glu Gln
500 505 510

Val Ile Gln Asp Ala Leu Asn Gln Leu Glu Glu Pro Pro Leu Ile
515 520 525

Ser Cys Ala Gly Ser Ala Asp His Leu Leu Ser Thr Val Thr Ser
530 535 540

Ile Ser Ser Cys Ile Glu Gln Leu Glu Lys Ser Trp Ser Gln Tyr
545 550 555

Leu Ala Cys Pro Glu Asp Ile Ser Gly Leu Leu His Ser Ile Thr
560 565 570

Leu Leu Ala His Leu Thr Ser Asp Ala Ile Ala His Gly Ala Thr
575 580 585

Thr Cys Leu Arg Ala Pro Pro Glu Pro Ala Asp Ser Leu Thr Glu
590 595 600

Ala Cys Lys Gln Tyr Gly Arg Glu Thr Leu Ala Tyr Leu Ala Ser
605 610 615

Leu Glu Glu Glu Gly Ser Leu Glu Asn Ala Asp Ser Thr Ala Met
620 625 630

Arg Asn Cys Leu Ser Lys Ile Lys Ala Ile Gly Glu Glu Leu Leu
635 640 645

Pro Arg Gly Leu Asp Ile Lys Gln Glu Glu Leu Gly Asp Leu Val
650 655 660

Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu Thr Cys Thr
665 670 675

Ala Arg Ile Glu Glu Met Leu Ser Lys Ser Arg Ala Gly Asp Thr
680 685 690

Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Arg Cys Cys Thr
695 700 705

Ser Leu Met Gln Ala Ile Gln Val Leu Ile Val Ala Ser Lys Asp
710 715 720

Leu Gln Arg Glu Ile Val Glu Ser Gly Arg Gly Thr Ala Ser Pro
725 730 735

Lys Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu Ile
740 745 750

Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Val Met Val Asp
765 770 775

Ala Ala Asp Leu Val Val Gln Gly Arg Gly Lys Phe Glu Glu Leu
780 785 790

Met Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala Gln Leu Val
795 800 805

```
Ala Ala Ser Lys Val Lys Ala Asp Lys Asp Ser Pro Asn Leu Ala
                810                 815                 820

Gln Leu Glu Gln Ala Ser Arg Gly Val Asn Gln Ala Thr Ala Gly
                825                 830                 835

Val Val Ala Ser Thr Ile Ser Gly Lys Ser Gln Ile Glu Glu Thr
                840                 845                 850

Asp Asn Met Asp Phe Ser Ser Met Thr Leu Thr Gln Ile Lys Arg
                855                 860                 865

Gln Glu Met Asp Ser Gln Val Arg Val Leu Glu Leu Glu Asn Glu
                870                 875                 880

Leu Gln Lys Glu Arg Gln Lys Leu Gly Glu Leu Arg Lys Lys His
                885                 890                 895

Tyr Glu Leu Ala Gly Val Ala Glu Gly Trp Glu Glu Gly Thr Glu
                900                 905                 910

Ala Ser Pro Pro Thr Leu Gln Glu Val Val Thr Glu Lys Glu
                915                 920                 924
```

(2) INFORMATION FOR SEQ ID NO: 5
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1090
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntinglin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

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Met Leu Leu Cys Gln Gly Ser Glu Trp Arg Arg Asp Gln Gln Leu
                  5                  10                  15

Gly Thr Ala Asn Ala Arg Gln Trp Cys Pro Leu Pro Gln Asp Ala
                 20                  25                  30

Gln Pro Ala Gly Ser Trp Glu Arg Cys Pro Pro Leu Pro Pro Ala
                 35                  40                  45

Gly Arg Leu Gln Gly Thr Asp His Pro Trp Gly Trp Gly Arg Leu
                 50                  55                  60
```

Ala Gly Gly Gly Glu Arg Gly Gly Leu Trp Glu Gly Leu Ser His
65 70 75

Ser Gln Arg Leu Ile His Leu Ile Leu Leu Ser Leu Pro Leu Leu
80 85 90

Val Phe Gln Thr Val Ser Ile Asn Lys Ala Ile Asn Thr Gln Glu
95 100 105

Val Ala Val Lys Glu Lys His Ala Arg Thr Cys Ile Leu Gly Thr
110 115 120

His His Glu Lys Gly Ala Gln Thr Phe Trp Ser Val Val Asn Arg
125 130 135

Leu Pro Leu Ser Ser Asn Ala Val Leu Cys Trp Lys Phe Cys His
140 145 150

Val Phe His Lys Leu Leu Arg Asp Gly His Pro Asn Val Leu Lys
155 160 165

Asp Ser Leu Arg Tyr Arg Asn Glu Leu Ser Asp Met Ser Arg Met
170 175 180

Trp Gly His Leu Ser Glu Gly Tyr Gly Gln Leu Cys Ser Ile Tyr
185 190 195

Leu Lys Leu Leu Arg Thr Lys Met Glu Tyr His Thr Lys Asn Pro
200 205 210

Arg Phe Pro Gly Asn Leu Gln Met Ser Asp Arg Gln Leu Asp Glu
215 220 225

Ala Gly Glu Ser Asp Val Asn Asn Phe Phe Gln Leu Thr Val Glu
230 235 240

Met Phe Asp Tyr Leu Glu Cys Glu Leu Asn Leu Phe Gln Thr Val
245 250 255

Phe Asn Ser Leu Asp Met Ser Arg Ser Val Ser Val Thr Ala Ala
260 265 270

Gly Gln Cys Arg Leu Ala Pro Leu Ile Gln Val Ile Leu Asp Cys
275 280 285

Ser His Leu Tyr Asp Tyr Thr Val Lys Leu Leu Phe Lys Leu His
290 295 300

Ser Cys Leu Pro Ala Asp Thr Leu Gln Gly His Arg Asp Arg Phe
305 310 315

Met Glu Gln Phe Thr Lys Leu Lys Asp Leu Phe Tyr Arg Ser Ser
320 325 330

Asn Leu Gln Tyr Phe Lys Arg Leu Ile Gln Ile Pro Gln Leu Pro
335 340 345

Glu Asn Pro Pro Asn Phe Leu Arg Ala Ser Ala Leu Ser Glu His
350 355 360

Ile Ser Pro Val Val Val Ile Pro Ala Glu Ala Ser Ser Pro Asp
365 370 375

Ser Glu Pro Val Leu Glu Lys Asp Asp Leu Met Asp Met Asp Ala
380 385 390

Ser Gln Gln Asn Leu Phe Asp Asn Lys Phe Asp Asp Ile Phe Gly
395 400 405

Ser Ser Phe Ser Ser Asp Pro Phe Asn Phe Asn Ser Gln Asn Gly
410 415 420

Val Asn Lys Asp Glu Lys Asp His Leu Ile Glu Arg Leu Tyr Arg
425 430 435

Glu Ile Ser Gly Leu Lys Ala Gln Leu Glu Asn Met Lys Thr Glu
440 445 450

Ser Gln Arg Val Val Leu Gln Leu Lys Gly His Val Ser Glu Leu
455 460 465

Glu Ala Asp Leu Ala Glu Gln Gln His Leu Arg Gln Gln Ala Ala
470 475 480

Asp Asp Cys Glu Phe Leu Arg Ala Glu Leu Asp Glu Leu Arg Arg
485 490 495

Gln Arg Glu Asp Thr Glu Lys Ala Gln Arg Ser Leu Ser Glu Ile
500 505 510

Glu Arg Lys Ala Gln Ala Asn Glu Gln Arg Tyr Ser Lys Leu Lys
515 520 525

Glu Lys Tyr Ser Glu Leu Val Gln Asn His Ala Asp Leu Leu Arg
530 535 540

Lys Asn Ala Glu Val Thr Lys Gln Val Ser Met Ala Arg Gln Ala
545 550 555

Gln Val Asp Leu Glu Arg Glu Lys Lys Glu Leu Glu Asp Ser Leu
560 565 570

Glu Arg Ile Ser Asp Gln Gly Gln Arg Lys Thr Gln Glu Gln Leu
575 580 585

Glu Val Leu Glu Ser Leu Lys Gln Glu Leu Ala Thr Ser Gln Arg
590 595 600

Glu Leu Gln Val Leu Gln Gly Ser Leu Glu Thr Ser Ala Gln Ser
605 610 615

Glu Ala Asn Trp Ala Ala Glu Phe Ala Glu Leu Glu Lys Glu Arg
620 625 630

Asp Ser Leu Val Ser Gly Ala Ala His Arg Glu Glu Glu Leu Ser
635 640 645

Ala Leu Arg Lys Glu Leu Gln Asp Thr Gln Leu Lys Leu Ala Ser
650 655 660

Thr Glu Glu Ser Met Cys Gln Leu Ala Lys Asp Gln Arg Lys Met
665 670 675

Leu Leu Val Gly Ser Arg Lys Ala Ala Glu Gln Val Ile Gln Asp
680 685 690

Ala Leu Asn Gln Leu Glu Glu Pro Pro Leu Ile Ser Cys Ala Gly
695 700 705

Ser Ala Asp His Leu Leu Ser Thr Val Thr Ser Ile Ser Ser Cys
710 715 720

Ile Glu Gln Leu Glu Lys Ser Trp Ser Gln Tyr Leu Ala Cys Pro
725 730 735

Glu Asp Ile Ser Gly Leu Leu His Ser Ile Thr Leu Leu Ala His
740 745 750

Leu Thr Ser Asp Ala Ile Ala His Gly Ala Thr Thr Cys Leu Arg
755 760 765

Ala Pro Pro Glu Pro Ala Asp Ser Leu Thr Glu Ala Cys Lys Gln
770 775 780

Tyr Gly Arg Glu Thr Leu Ala Tyr Leu Ala Ser Leu Glu Glu Glu
785 790 795

Gly Ser Leu Glu Asn Ala Asp Ser Thr Ala Met Arg Asn Cys Leu
800 805 810

Ser Lys Ile Lys Ala Ile Gly Glu Glu Leu Leu Pro Arg Gly Leu
815 820 825

Asp Ile Lys Gln Glu Glu Leu Gly Asp Leu Val Asp Lys Glu Met
830 835 840

Ala Ala Thr Ser Ala Ala Ile Glu Thr Ala Thr Ala Arg Ile Glu
845 850 855

Glu Met Leu Ser Lys Ser Arg Ala Gly Asp Thr Gly Val Lys Leu
860 865 870

Glu Val Asn Glu Arg Ile Leu Gly Cys Cys Thr Ser Leu Met Gln
875 880 885

Ala Ile Gln Val Leu Ile Val Ala Ser Lys Asp Leu Gln Arg Glu
890 895 900

Ile Val Glu Ser Gly Arg Gly Thr Ala Ser Pro Lys Glu Phe Tyr
905 910 915

Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu Ile Ser Ala Ser Lys
920 925 930

Ala Val Gly Trp Gly Ala Thr Val Met Val Asp Ala Ala Asp Leu
935 940 945

Val Val Gln Gly Arg Gly Lys Phe Glu Glu Leu Met Val Cys Ser
950 955 960

His Glu Ile Ala Ala Ser Thr Ala Gln Leu Val Ala Ala Ser Lys
965 970 975

Val Lys Ala Asp Lys Asp Ser Pro Asn Leu Ala Gln Leu Gln Glu
980 985 990

Ala Ser Arg Gly Val Asn Gln Ala Thr Ala Gly Val Val Ala Ser
995 1000 1005

Thr Ile Ser Gly Lys Ser Gln Ile Glu Glu Thr Asp Asn Met Asp
1010 1015 1020

Phe Ser Ser Met Thr Leu Thr Gln Ile Lys Arg Gln Glu Met Asp
1025 1030 1035

Ser Gln Val Arg Val Leu Glu Leu Glu Asn Glu Leu Gln Lys Glu
1040 1045 1050

Arg Gln Lys Leu Gly Glu Leu Arg Lys Lys His Tyr Glu Leu Ala
1055 1060 1065

Gly Val Ala Glu Gly Trp Glu Glu Gly Thr Glu Ala Ser Pro Pro
1070 1075 1080

Thr Leu Gln Glu Val Val Thr Glu Lys Glu
1085 1090

(2) INFORMATION FOR SEQ ID NO:6:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3301
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 6:

CGGTGAGCTC GAGGAGCAGC GGAAGCAGAA GCAGAAGGCC CTGGTGGATA 50
ATGAGCAGCT CCCCCACGAG CTGGCCCAGC TGAGGGCTGC CCAGCTGGAG 100
CGCGAGCGGA GCCAGGGCCT GCGTGAGGAG GCTCAGAGGA AGGCCAGTGC 150
CACGGAGGCG CGCTACAACA AGCTGAAGGA AAACCACAGT GAGCTCGTCC 200
ATGTGCACGC GGAGCTGCTC AGAAAGAACG CGGACACAGC CAAGCAGCTG 250
ACGGTGACGC AGCAAAGCCA GGAGGAGGTG GCGCGGGTGA AGCAGCAGCT 300
GGCCTTCCAC GTGGAGCAGG TGAAGCGGGA GTCGGAGTTG AAGCTAGAGC 350
AGAAGAGCGA CCAGCAGGAG AAGCTCAAGA GGGAGCTGGA GGCCAAGGCC 400
GGAGAGCTGG CCCCGCGCGA GGAGGCCCTG AGCCACACAG AGCAGAGCAA 450
GTCGGAGCTG AGCTCACGGC TGGACACACT GAGTGCGGAG AAGGATGCTC 500
TGAGTGGAGC TGTGCGGCAG CGGGAGGCAG ACCTGCTGGC GGCGCAGAGC 550
CTGGTGCGCG AGACAGAGGC GGCGCTGAGC CGGCAGCAGC AGCGCAGCTC 600
CCAGGAGCAG GGCGAGTTGC AGGGCCGGCT GGCAGAGAGG GAGTCTCAGG 650
AGCAGGGGCT GCGGCAGAGG CTGCTGGACG AGCAGTTCGC AGTGTTGCGG 700
GGCGCTGCTG CCGAGGCCGC GGGCATCCTG CAGGATGCCG TGAGCAAGCT 750
GGACGACCCC CTGCACCTGC GCTGTACCAG CTCCCCAGAC TACCTGGTGA 800
GCAGGGCCCA GGAGGCCTTG GATGCCGTGA GCACCCTGGA GGAGGGCCAC 850
GCCCAGTACC TGACCTCCTT GGCAGACGCC TCCGCCCTCC TGGCAGCTCT 900
GACCCGCTTC TCCCACCTGG CTGCGGATAC CATCATCAAT GGCGGTGCCA 950
CCTCGCACCT GGCTCCCACC GACCCTGCCG ACCGCCTCAT AGACACCTGC 1000
AGGGAGTGCG GGGCCCGGGC TCTGGAGCTC ATGGGGCAGC TGCAGGACCA 1050
GCAGGCTCTG CGGCACATGC AGGCCAGCCT GGTGCGGACA CCCCTGCAGG 1100
GCATCCTTCA GCTGGGCCAA GAACTGAAAC CCAAGAGCCT AGATGTGCGG 1150
CAGGAGGAGC TGGGGGCCGT GGTCGACAAG GAGATGGCGG CCACATCCGC 1200
AGCCATTGAA GATGCTGTGC GGAGGATTGA GGACATGATG AACCAGGCAC 1250
GCCACGCCAG CTCGGGGCTG AAGCTGGAGG TGAACGAGAG GATCCTCAAC 1300
TCCTGCACAG ACCTGATGAA GCCTATCCGG CTCCTGGTGA CGACATCCAC 1350
TAGCCTGCAG AAGGAGATCG TGGAGAGCGC CAGGGGGGCA GCCACGCAGC 1400
AGGAATTTTA CGCCAAGAAC TCGCGCTGGA CCGAAGCCCT CATCTCGGCC 1450
TCCAAGGCTG TGGGCTGGGG AGCCACACAG CTGGTGGAGG CAGCTGACAA 1500
GGTGGTGCTT CACACGGGCA AGTATGAGGA GCTCATCGTC TGCTCCCACG 1550
AGATCGCAGC CAGCACGGCC CAGCTGGTGG CGGCCTCCAA GGTGAAGGCC 1600

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AACAAGCACA GCCCCCACCT GAGCCCCCTG CAGGAATGTT CTCGCACAGT 1650
CAATGAGAGG GCTGCCAATG TGGTGGCCTC CACCAAGTCA GGCCAGGAGC 1700
AGATTGAGCA CAGAGACACC ATGGATTTCT CCGGCCTGTC CCTCATCAAG 1750
CTGAAGAAGC AGGAGATGGA GACCCAGCTG CGTGTCCTGG AGCTGGAGAA 1800
GACGCTGGAG GCTGAACGCA TCCGGCTGGG GGAGTTGCGG AAGCAACACT 1850
ACGTGCTGGC TGGGGCATCA GGCAGCCCTG GAGAGGAGGT GGCCATCCGG 1900
CCCAGCACTG CCCCCCGAAG TGTAACCACC AAGAAACCAC CCCTGGCCCA 1950
GAAGCCCAGC GTGGCCCCCA GACAGGACCA CCAGCTTGAC AAAAAGGATG 2000
GCATCTACCC AGCTCAACTC GTGAACTACT AGGCCCCCCA GGGGTCCAGC 2050
AGGGTGGCTG GTGACAGGCC TGGGCCTCTG CAACTGCCCT GACAGGACCG 2100
AGAGGCCTTG CCCCTCCACC TGGTCCCCAA GCCTCCCGCC CCACCGTCTG 2150
GATCAATGTC CTCAAGGCCC CTGGCCCTTA CTGAGCCTGC AGGGTCCTGG 2200
GCCATGTGGG TGGTGCTTCT GGATGTGAGT CTCTTATTTA TCTGCAGAAG 2250
GAACTTTGGG GTGCAGCCAG GACCCGGTAG GCCTGAGCCT CAACTCTTCA 2300
GAAAATAGTG TTTTTAATAT TCCTCTTCAG AAAATAGTGT TTTTAATATT 2350
CCGAGCTAGA GCTCTTCTTC CTACGTTTGT AGTCAGCACA CTGGGAAACC 2400
GGGCCAGCGT GGGCCTCCCT GCCTTCTGGA CTCCTGAAGG TCGTGGATGG 2450
ATGGAAGGCA CACAGCCCGT GCCGGCTGAT GGGACGAGGG TCAGGCATCC 2500
TGTCTGTGGC CTTCTGGGGC ACCGATTCTA CCAGGCCCTC CAGCTGCGTG 2550
GTCTCCGCAG ACCAGGCTCT GTGTGGGCTA GAGGAATGTC GCCCATTACC 2600
TCCTCAGGCC CTGGCCCCTCG GGCCTCCGTG ATGGGAGCCC CCCAGGAGGG 2700
GTCAGATGCT GGAAGGGGCC GCTTTCTGGG GAGTGAGGTG AGACATAGCG 2750
GCCCAGGCGC TGCCTTCACT CCTGGAGTTT CCATTTCCAG CTGGAATCTG 2800
CAGCCACCCC CATTTCCTGT TTTCCATTCC CCCGTTCTGG CCGCGCCCCA 2850
CTGCCCACCT GAAGGGGTGG TTTCCAGCCC TCCGGAGAGT GGGCTTGGCC 2900
CTAGGCCCTC CAGCTCAGCC AGAAAAAGCC CAGAAACCCA GGTGCTGGAC 2950
CAGGGCCCTC AGGGAGGGAC CCTGCGGCTA GAGTGGGCTA GGCCCTGGCT 3000
TTGCCCGTCA GATTTGAACG AATGTGTGTC CCTTGAGCCC AAGGAGAGCG 3050
GCAGGAGGGG TGGGACCAGG CTGGGAGGAC AGAGCCAGCA GCTGCCATGC 3100
CCTCCTGCTC CCCCCACCCC AGCCCTAGCC CTTTAGCCTT TCACCCTGTG 3150
CTCTGGAAAG GCTACCAAAT ACTGGCCAAG GTCAGGAGGA GCAAAAATGA 3200
GCCAGCACCA GCGCCTTGGC TTTGTGTTAG CATTTCCTCC TGAAGTGTTC 3250
TGTTGGCAAT AAAATGCACT TTCACTGTTA AAAAAAAAAA AAAAAAAAAA 3300
A                                                       3301
```

(2) INFORMATION FOR SEQ ID NO: 7
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 676
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

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Gly Glu Leu Glu Glu Gln Arg Lys Gln Lys Gln Lys Ala Leu Val
 5                  10                  15
```

Asp Asn Glu Gln Leu Arg His Glu Leu Ala Gln Leu Arg Ala Ala
20 25 30

Gln Leu Glu Arg Glu Arg Ser Gln Gly Leu Arg Glu Glu Ala Glu
35 40 45

Arg Lys Ala Ser Ala Thr Glu Ala Arg Tyr Asn Lys Leu Lys Glu
50 55 60

Lys His Ser Glu Leu Val His Val His Ala Glu Leu Leu Arg Lys
65 70 75

Asn Ala Asp Thr Ala Lys Gln Leu Thr Val Thr Gln Gln Ser Gln
80 85 90

Glu Glu Val Ala Arg Val Lys Glu Gln Leu Ala Phe Gln Val Glu
95 100 105

Gln Val Lys Arg Glu Ser Glu Leu Lys Leu Glu Glu Lys Ser Asp
110 115 120

Gln Gln Glu Lys Leu Lys Arg Glu Leu Glu Ala Lys Ala Gly Glu
125 130 135

Leu Ala Arg Ala Gln Glu Ala Leu Ser His Thr Glu Gln Ser Lys
140 145 150

Ser Glu Leu Ser Ser Arg Leu Asp Thr Leu Ser Ala Glu Lys Asp
155 160 165

Ala Leu Ser Gly Ala Val Arg Gln Arg Glu Ala Asp Leu Leu Ala
170 175 180

Ala Gln Ser Leu Val Arg Glu Thr Glu Ala Ala Leu Ser Arg Glu
185 190 195

Gln Gln Arg Ser Ser Gln Glu Gln Gly Glu Leu Gln Gly Arg Leu
200 205 210

Ala Glu Arg Glu Ser Gln Glu Gln Gly Leu Arg Gln Arg Leu Leu
215 220 225

Asp Glu Gln Phe Ala Val Leu Arg Gly Ala Ala Ala Glu Ala Ala
230 235 240

Gly Ile Leu Gln Asp Ala Val Ser Lys Leu Asp Asp Pro Leu His
245 250 255

Leu Arg Cys Thr Ser Ser Pro Asp Tyr Leu Val Ser Arg Ala Gln
260 265 270

Glu Ala Leu Asp Ala Val Ser Thr Leu Glu Glu Gly His Ala Gln
275 280 285

Tyr Leu Thr Ser Leu Ala Asp Ala Ser Ala Leu Val Ala Ala Leu
290 295 300

Thr Arg Phe Ser His Leu Ala Ala Asp Thr Ile Ile Asn Gly Gly
305 310 315

Ala Thr Ser His Leu Ala Pro Thr Asp Pro Ala Asp Arg Leu Ile
320 325 330

Asp Thr Cys Arg Glu Cys Gly Ala Arg Ala Leu Glu Leu Met Gly
335 340 345

Gln Leu Gln Asp Gln Gln Ala Leu Arg His Met Gln Ala Ser Leu
350 355 360

Val Arg Thr Pro Leu Gln Gly Ile Leu Gln Leu Gly Gln Glu Leu
365 370 375

Lys Pro Lys Ser Leu Asp Val Arg Gln Glu Glu Leu Gly Ala Val
380 385 390

Val Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu Asp Ala
395 400 405

Val Arg Arg Ile Glu Asp Met Met Asn Gln Ala Arg His Ala Ser
410 415 420

Ser Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Asn Ser Cys
425 430 435

Thr Asp Leu Met Lys Ala Ile Arg Leu Leu Val Thr Thr Ser Thr
440 445 450

Ser Leu Gln Lys Glu Ile Val Glu Ser Gly Arg Gly Ala Ala Thr
455 460 465

Gln Gln Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu
470 475 480

Ile Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Gln Leu Val
485 490 495

Glu Ala Ala Asp Lys Val Val Leu His Thr Gly Lys Tyr Glu Glu
500 505 510

Leu Ile Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala Gln Leu
515 520 525

```
Val Ala Ala Ser Lys Val Lys Ala Asn Lys His Ser Pro His Leu
                530                 535                 540

Ser Arg Leu Gln Glu Cys Ser Arg Thr Val Asn Glu Arg Ala Ala
                545                 550                 555

Asn Val Val Ala Ser Thr Lys Ser Gly Gln Glu Gln Ile Glu Asp
                560                 565                 570

Arg Asp Thr Met Asp Phe Ser Gly Leu Ser Leu Ile Lys Leu Lys
                575                 580                 585

Lys Gln Glu Met Glu Thr Gln Val Arg Val Leu Glu Leu Glu Lys
                590                 595                 600

Thr Leu Glu Ala Glu Arg Met Arg Leu Gly Glu Leu Arg Lys Gln
                605                 610                 615

His Tyr Val Leu Ala Gly Ala Ser Gly Ser Pro Gly Glu Glu Val
                620                 625                 630

Ala Ile Arg Pro Ser Thr Ala Pro Arg Ser Val Thr Thr Lys Lys
                635                 640                 645

Pro Pro Leu Ala Gln Lys Pro Ser Val Ala Pro Arg Gln Asp His
                650                 655                 660

Gln Leu Asp Lys Lys Asp Gly Ile Tyr Pro Ala Gln Leu Val Asn
                665                 670                 675

Tyr
```

(2) INFORMATION FOR SEQ ID NO:8:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2338
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: cDNA for Huntingtin-interacting protein - mHIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 8:

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GGCACGAGGG CTCATTCAGA TCCCCCAGCT GCCCGAGAAT CCACCCAACTT    50
CCTACGAGCC TCGGCCCTGT CAGAGCACAT CAGTCCTGTG GTGGTGATCCC   100
GGCAGAGGTG TCATCCCCAG ACAGTGAGCC TGTCCTGGAG AAGGATGACCT   150
CATGGACATG GACGCCTCCC AGCAGACTTT GTTTGACAAC AAGTTTCATGA   200
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CGTCTTTGGC AGCTCATTCA GCAGCGACCC TTTCAATTTC AACAATCAAAA  250
TGGCGTGAAC AAGGACGACA AGGACCACTT GATTGAACGC CTGTACAGAGA  300
GATCAGTGGA CTGACAGGCC AGCTGGACAA CATGAAGATT GAGAGCCAGCG  350
GGCCATGCTG CAGCTGAAGG GTCGAGTGAG TGAGCTGGAG GCAGAGCTAGC  400
AGAGCAGCAG CACTTGGGCC GGCAGGCTAT GGATGACTGC GAGTTCCTGCG  450
CACTGAGCTG GATGAACTGA AGAGGCAGCG AGAGGACACG GAGAAGGCACA  500
GCGCAGCCTG ACTGAGATAG AAAGAAAGGC CCAGGCTAAT GAACAGAGGTA  550
TAGCAAGTTA AAAGACAAGT ACAGTGAACT GGTCCACAAC CATCCTGACCT  600
GCTGCGGAAG AACGCAGACG TGACCAAACA GGTCTCCCTG GCCCGCCAACC  650
CCAGGTGGAT TTGGAAAGAG AGAAAAAAGA GCTAGCAGAT TCCTTTGCAC  700
GTGTAAGTGA CCAGGCCCAG CGGAAGACTC AAGAGCAACA GGATGTTCTA  750
GAGAACCTGA AGCATGAACT GGCCACCAGC AGACAGGAGC TGCAGGTCCT  800
CCACAGCAAC CTGGAAACCT CTGCCCAGTC AGAAGCGAAA TGGCTGACAC  850
AGATCCCCGA GTTGGAGAAG GAACAAGGCA GCTTGGCGAC TGTTGCAGCT  900
CAGAGAGACG AAGAGTTATC AGCCCTCCGA GACCAGCTGG AAAGCACCCA  950
GATCAAGCTG GCTGGCGCCC AGGAATCCAT GTGCCAGCAC CTGAACGACC 1000
AGAGGAAAAC CCTCTTGGCA CCGATCAGGA ACCCTGCGGA GCGTGAGATA 1050
CAGGAGGCGC TGAGCCAGCT TGAGGAACCC ACCCTCATCA GCTGTGCAGG 1100
ATCCACAGAT CACCTTCTCT CCAAAGTCAG CTCCGTTTCC AGCTGCCTCG 1150
AGCAACTGGA AAAGAACGGC AGCCAGTATC TGGCCTGCCC AGAAGATATT 1200
AGTGAGCTTC TGCACTCGAT CACCCTGCTT GCCCACTTGA CCGGTGACAC 1250
TGTCATCCAG GGGAGTGCCA CCAGCCTCCG GGCCCCACCG GAGCCAGCCG 1300
ACTCGTTGAC CGAGGCCTGT AGGCAGTATG GCAGAGAAAC CCTGGCCTAT 1350
CTGTCCTCCC TGGAGGAAGA GGGAACTGTG GAGAATGCTG ACGTCACAGC 1400
CCTTAGGAAT TGCCTCAGCA CCCTCAAGAC CCTTGGCGAG CAGCTGCTGC 1450
CCAGGGGCCT GGACATCAAG CAGGAAGAGC TGGGTGACCT GGTGGACAAG 1500
GAGATGGCAG CCACTTCAGC TGCCATTGAA GCTGCCACCA CCCCGATAGA 1550
GGAAATTCTC AGTAAGTCCC GAGCAGGAGA CACGGGAGTC AAGCTGGAGG 1600
TGAATGAGAG GATCCTGGGT TCCTGTACCA GCCTGATGCA GGCCATCAAG 1650
GTGCTCGTTG TGGCCTCCAA GGACCTCCAG AAGGAGATAG TGGAGAGTGG 1700
CAGGGGTAGT GCATCCCCTA AAGAATTTTA CGCCAAGAAC TCTCGGTGGA 1750
CGGAAGGGCT GATATCCGCC TCCAAACCTC TTGGTTGGGG AGCTACCATC 1800
ATGGTGGATG CTGCTGATCT TGTGGTCCAA GCCAAACGCA AGTTCGAGGA 1850
GCTGATCGTG TGTTCACGCG AGATTGCTGC CAGTACTGCC CAGCTCCTCC 1900
CTGCATCCAA CCTGAAAGCG AACAAGGGCA GCCTCAATCT GACCCAGCTG 2000
CAGCAGGCCT CTCGAGGACT GAACCAGGCC ACAGCCGCTG TGGTGGCCTC 2050
AACCATTTCT GGCAAATCTC AGATTGAGGA AACAGACAGT ATGGACTTCT 2100
CAAGCATGAC ACTGACCCAG ATCAAGCGCC AGGAGATGGA TTCCCAGGTT 2150
AGGGTGCTGG AGCTGGAAAA TGACCTGCAG AAGGAGCGTC AGAAACTAGG 2200
AGAGCTACGG AAGAAACACT ACGAGCTGGA GGGCGTGGCT GAGGGCTGGG 2250
AGGAAGGGAC AGAAGCATCA CCGTCTACTG TCCAAGAAGC AATACCGGAC 2300
AAAGAGTAGA GCCAAGCCGA CACCCCACAC ATCAGAAA              2338
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(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 676

(B) TYPE: protein

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: protein

(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

Ala Arg Gly Leu Ile Gln Ile Pro Gln Leu Pro Glu Asn Pro Pro
5 10 15

Asn Phe Leu Arg Ala Ser Ala Leu Ser Glu His Ile Ser Pro Val
20 25 30

Val Val Ile Pro Ala Glu Val Ser Ser Pro Asp Ser Glu Pro Val
35 40 45

Leu Glu Lys Asp Asp Leu Met Asp Met Asp Ala Ser Gln Gln Thr
50 55 60

Leu Phe Asp Asn Lys Phe Asp Asp Val Phe Gly Ser Ser Leu Ser
65 70 75

Ser Asp Pro Phe Asn Phe Asn Asn Gln Asn Gly Val Asn Lys Asp
80 85 90

Glu Lys Asp His Leu Ile Glu Arg Leu Tyr Arg Glu Ile Ser Gly
95 100 105

Leu Thr Gly Gln Leu Asp Asn Met Lys Ile Glu Ser Gln Arg Ala
110 115 120

Met Leu Gln Leu Lys Gly Arg Val Ser Glu Leu Glu Ala Glu Leu
125 130 135

Ala Glu Gln Gln His Leu Gly Arg Gln Ala Met Asp Asp Cys Glu
140 145 150

Phe Leu Arg Thr Glu Leu Asp Glu Leu Lys Arg Gln Arg Glu Asp
155 160 165

Thr Glu Lys Ala Gln Arg Ser Leu Thr Glu Ile Glu Arg Lys Ala
170 175 180

Gln Ala Asn Glu Gln Arg Tyr Ser Lys Leu Lys Glu Lys Tyr Ser
185 190 195

Glu Leu Val Gln Asn His Ala Asp Leu Leu Arg Lys Asn Ala Glu
200 205 210

Val Thr Lys Gln Val Ser Val Ala Arg Gln Ala Gln Val Asp Leu
215 220 225

Glu Arg Glu Lys Lys Glu Leu Ala Asp Ser Phe Ala Arg Val Ser

230 235 240

Asp Gln Ala Gln Arg Lys Thr Gln Glu Glu Gln Asp Val Leu Glu
245 250 255

Asn Leu Lys His Glu Leu Ala Thr Ser Arg Gln Glu Leu Gln Val
260 265 270

Leu His Ser Asn Leu Glu Thr Ser Ala Gln Ser Glu Ala Lys Trp
275 280 285

Leu Thr Gln Ile Ala Glu Leu Glu Lys Glu Gln Gly Ser Leu Ala
290 295 300

Thr Val Ala Ala Gln Arg Glu Glu Glu Leu Ser Ala Leu Arg Asp
305 310 315

Gln Leu Glu Ser Thr Gln Ile Lys Leu Ala Gly Ala Gln Glu Ser
320 325 330

Met Cys Gln Gln Val Lys Asp Gln Arg Lys Thr Leu Leu Ala Gly
335 340 345

Ile Arg Lys Ala Ala Glu Arg Glu Ile Gln Glu Ala Leu Ser Gln
350 355 360

Leu Glu Glu Pro Thr Leu Ile Ser Cys Ala Gly Ser Thr Asp His
365 370 375

Leu Leu Ser Lys Val Ser Ser Val Ser Ser Cys Leu Glu Gln Leu
380 385 390

Glu Lys Asn Gly Ser Gln Tyr Leu Ala Cys Pro Glu Asp Ile Ser
395 400 405

Glu Leu Leu His Ser Ile Thr Leu Leu Ala His Leu Thr Gly Asp
410 415 420

Thr Val Ile Gln Gly Ser Ala Thr Ser Leu Arg Ala Pro Pro Glu
425 430 435

Pro Ala Asp Ser Leu Thr Glu Ala Cys Arg Gln Tyr Gly Arg Glu
440 445 450

Thr Leu Ala Tyr Leu Ser Ser Leu Glu Glu Glu Gly Thr Val Glu
455 460 465

Asn Ala Asp Val Thr Ala Leu Arg Asn Cys Leu Ser Arg Val Lys
470 475 480

Thr Leu Gly Glu Glu Leu Leu Pro Arg Gly Leu Asp Ile Lys Gln
485 490 495

Glu Glu Leu Gly Asp Leu Val Asp Lys Glu Met Ala Ala Thr Ser
500 505 510

Ala Ala Ile Glu Ala Ala Thr Thr Arg Ile Glu Glu Ile Leu Ser
515 520 525

Lys Ser Arg Ala Gly Asp Thr Gly Val Lys Leu Glu Val Asn Glu
530 535 540

Arg Ile Leu Gly Ser Cys Thr Ser Leu Met Gln Ala Ile Lys Val
545 550 555

Leu Val Val Ala Ser Lys Asp Leu Gln Lys Glu Ile Val Glu Ser
560 565 570

Gly Arg Gly Ser Ala Ser Pro Lys Glu Phe Tyr Ala Lys Asn Ser
575 580 585

Arg Trp Thr Glu Gly Leu Ile Ser Ala Ser Lys Ala Val Gly Trp
590 595 600

Gly Ala Thr Ile Met Val Asp Ala Ala Asp Leu Val Val Gln Gly
605 610 615

Lys Gly Lys Phe Glu Glu Leu Met Val Cys Ser Arg Glu Ile Ala
620 625 630

Ala Ser Thr Ala Gln Leu Val Ala Ala Ser Lys Val Lys Ala Asn
635 640 645

Lys Gly Ser Leu Asn Leu Thr Gln Leu Gln Glu Ala Ser Arg Gly
650 655 660

Val Asn Gln Ala Thr Ala Ala Val Val Ala Ser Thr Ile Ser Gly
665 670 675

Lys Ser Gln Ile Glu Glu Thr Asp Ser Met Asp Phe Ser Ser Met
680 685 690

Thr Leu Thr Gln Ile Lys Arg Gln Glu Met Asp Ser Gln Val Arg
695 700 705

Val Leu Glu Leu Glu Asn Asp Leu Gln Lys Glu Arg Gln Lys Leu
710 715 720

Gly Glu Leu Arg Lys Lys His Tyr Glu Leu Glu Gly Val Ala Glu
725 730 735

Gly Trp Glu Glu Gly Thr Glu Ala Ser Pro Ser Thr Val Gln Glu
740 745 750

Ala Ile Pro Asp Lys Glu
755

(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3964
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: cDNA for Huntingtin-interacting protein - mHIP1a
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 10:

GGCACGAGGC GGCGCGCGGC CTCCGTGTGC CTAGGCTTGA GGCGGGCGGT 50
GACGCCTCAT TCGCGCGGAG CCGGGCCGGG ACACGGTCGC CGCCAGCATC 100
AACAGCATCA AGAATGTGCC GGCGCGGGTC CTGAGCCGCA GGCCGGGCCA 150
CAGCCTAGAG GCCGAGCGCG AGCAGTTCGA CAAGACGCAG GCCATCAGTA 200
TCAGCAAAGC CATCAACAGC CAGGAGGCCC CAGTGAAGGA GAAGCATGCC 250
CGGCGTATCA TCCTGGGCAC GCATCATGAG AAGGGAGCCT TCACCTTCTG 300
GTCCTATGCC ATCGGCCTGC CGCTGTCCAG CAGCTCCATC CTCAGCTGGA 350
AGTTCTGTCA CGTCCTTCAC AAGGTCCTCC GGGACGGACA CCCCAACGTC 400
CTGCATGACT ATCAGCGGTA CCGGAGCAAC ATACCTGAGA TCGGTGACTT 450
GTGGGGCCAC CTTCGTGACC AGTATGGACA CCTCGTGAAT ATCTATACCA 500
AACTGTTGCT GACTAAGATC TCCTTCCACC TTAAGCACCC CCAGTTTCCT 550
GCAGGCCTGG AGGTAACAGA TGACCTGTTG GAGAAGGCGG CGGGAACTGA 600
TGTCAACAAC ATTTTTCAGC TTACCGTGGA GATGTTTGAC TACATGGACT 650
GTGAACTGAA GCTTTCTGAG TCAGTTTTCC GGCAGCTCAA CACGGCCATC 700
GCAGTGTCCC AGATGTCTTC TGGCCAGTGT CGCCTAGCGC CGCTCATCCA 750
GGTCATTCAG GACTGCAGCC ACCTGTACCA CTACACAGTG AAGCTCATGT 800
TTAAGCTGCA CTCCTGTCTC CCGGCAGACA CCCTGCAAGG CCACAGGGAT 850
CGGTTCCACC AGCAGTTCCA CAGCCTCAAA AACTTCTTCC GCCGGGCTTC 900
AGACATGCTG TACTTCAAGA GGCTCATCCA GATCCCGCGG CTGCCTGAGG 950
GACCCCCCAA TTTCCTGCGG GCTTCAGCCC TGGCTGAGCA CATCAAGCCG 1000
GTGGTGGTGA TTCCCGAGGA GGCCCCAGAG GAAGAGGAGC CTGAGAACCT 1050
AATTGAAATC AGCAGTGCGC CCCCTGCTGC GGACCCACTG GTCGTCGCTG 1100
ACCTCTTTGA TCAGACCTTT GGACCCCCCA ATGGCTCCAT GAAGGATGAC 1150
AGGGACCTCC AAATCGAGAA CTTGAAGAGA GAGGTGGAGA CCCTCCGTGC 1200
TGAGCTGGAG AAGATTAAGA TGGAGGCACA CCCCTACATC TCCCAGCTGA 1250
AGGGCCAGGT GAATGGCCTG GAGGCAGAGC TGGAGGAGCA GCCCAACCAC 1300
AAGCAGAAGG CCCTGGTGCA CAACGAGCAG CTGCGCCACG AGCTGGCCCA 1350
GCTCAAGGCC CTGCAGCTGG AGGGCGCCCG CAACCAGGGC CTTCGAGAGG 1400
AAGCAGAGAG GAAGGCCAGT GCCACGGAGG CACGCTACAG CAAGCTGAAG 1450
GAGAAACACA GCGAACTCAT TAACACGCAC GCCGAGCTGC TCAGGAAGAA 1500

CGCAGACACG GCCAAGCAGC TGACAGTGAC ACAGCAGAGC CAGGAGGAGG 1550
TGGCACGGCT AAAGGAACAG CTGGCCTTCC AGATGGAGCA AGCGAAGCGT 1600
GAGTCTGAGA TGAAGATGGA AGAGCAGAGC GACCAGTTGG AGAAGCTCAA 1650
GAGGGAGCTG GCGCCCAGGG CACCAGAGCT GGCCCCTGCC CACGAGGCCC 1700
TGAGCCGCAC AGAACACACT GGGTCAGAGC TGAGCTCACC GCTGGACACA 1750
CTGAACGCGG AGAAGGAACC CCTGACTGGA GTCGTTCGGC AGCGTGAGGC 1800
AGAGCTGCTG GCCGCTCACA GCCTCCTCCG GGAGAAGGAG GAGGCGCTTA 1850
GCCAAGAGCA GCAGCGGAGC TCCCAGGAGA AGGGCGAGCT ACGGGGGCAG 1900
CTGGCAGAAA AGGAGTCTCA GGAGCAGAGG CTTCGGCAGA AGCTGCTGGA 1950
TGAGCAGTTG GCGGTGTTGC GAAGTGCAGC CGCCGAGGCA GAGGCCATCC 2000
TACAGGATGC AGTGAGCAAG CTGGACGACC CCCTGCACCT CCGCTGCACC 2050
AGCTCCCCAG ACTACTTGGT GAGCCGGGCT CAGGCAGCCC TGGACAGCGT 2100
GAGCGGCCTG GAGCAGGGCC ACACCCAGTA CCTGGCTTCC TCCGAAGATG 2150
CTTCTGCCCT GGTGGCAGCG CTGACCCGCT TCTCCCATTT GGCTGCGGAC 2200
ACCATTGTCA ATGGTGCCGC CACCTCCCAC CTGGCCCCCA CCGACCCCGC 2250
CGACCGCCTG ATGGACACAT GCAGGGAGTG TGGAGCCCGG GCTCTGGAGC 2300
TGGTGGGACA GCTGCAAGAC CAGACAGTGC TACGGAGGGC TCAGCCCAGC 2350
CTGATGCGGG CCCCCCTGCA GGGCATTCTG CAGTTGGGCC AGGACTTGAA 2400
GCCTAAGAGC CTGGATGTAC GGCAAGAGGA GCTAGGGGCC ATGGTGGACA 2450
AGGAGATGGC GGCCACCTCG GCAGCCATTG AGGACGCTCT CCCGAGGATC 2500
GAGGACATGA TGAGCCAGGC CCGCCACCAG AGCTCAGGCG TGAAACTGGA 2550
GGTGAATGAG AGGATCCTCA ACTCCTGCAC AGACCTGATG AAGGCTATCC 2600
GGCTCCTGGT GATGACCTCC ACCAGCCTGC AGAAGGAAAT TGTGGAGAGC 2650
GGCAGGGGGC CAGCAACGCA GCAGGAATTT TATGCCAAGA ATTCACGGTG 2700
GACTGAAGGC CTCATCTCAG CCTCTAAGGC AGTGGGCTGG GGAGCCACAC 2750
AGCTGGTGGA GTCACCTGAC AAGGTTGTGC TTCACATGGG CAAATACGAG 2800
GAACTCATCG TCTCCTCCCA TGAGATTGCG GCCAGCACGG CCCAGCTGGT 2850
GGCAGCCTCG AAGGTGAAAG CCAACAAGAA CAGTCCCCAC TTGAGCCGCC 2900
TGCAGGAATG TTCCCGCACT GTCAACGAGA GGGCTGCCAA CGTCGTGGCC 2950
TCCACCAAAT CTGGCCAGGA GCAGATTGAG GACAGAGACA CCATGGATTT 3000
CTCTGGCCTG TCCCTCATCA AGTTGAAGAA GCAGGAGATG GAGACACAGG 3050
TGCGAGTCTT GGAGCTGGAG AAGACACTAG AGGCAGAGCG TGTCCGGCTC 3100
GGGGAGCTTC GGAAACAGCA CTATGTACTG GCTGGGGGGA TGGGAACACC 3150
TAGCGAAGAA GAACCCAGCA GACCCAGCCC AGCTCCCCGA AGTGGGGCCA 3200
CTAAGAAGCC ACCGCTGGCC CAGAAACCCA CCATAGCCCC CAGGACAGAC 3250
AACCAGCTCGA CAAAAAGGAT GGTGTCTACC CAGCTCAACT TCTCAACTAC 3300
TAGGCCCCTAA GGTGTTCAGC AGGATGGCTG GTGGTTGTGC CTGCCCTTCA 3350
TGTGGCTGTCT GGCAGTGGTC AAGGGGCCTC TGAGAAGCCT CCAACTCCTG 3400
CCCAAGGGGCC TAGTCTGTGG GACAGTTCAT CTGGATGTGA ATCTATTTAT 3450
CTTAAGTAGGA ACTGCCTCGA GCAGCTGGGA CCCAGCAGGC CTGAGCCACA 3500
AATCTGCAGCG GACATCAGAG ATAGTCTGAA TGCTGCGAGG TATTTCTTTC 3550
TTCGTAAGTTT AGTCAGCACA CTGGGAAAAG GTCACATAAG CCAGGAGCCT 3600
CCTTGTCTCTG GACTCAAAAG TCTGAGGCCT TAAGTGAACA ACAGAAAGAG 3650
GGTCCCTGCTG GCTACCAGGG ATAAGGGGAT GACCTGTGAC CCTTGAGCCA 3700
GGGAGAGCAGG TAAGCTGGCT GGTGTCATCA CCTGGGGGCC TGGTGCTAGG 3750
GCATCCATGCT GGGAGCCCCA GCAGACCAGG CTTTGTGTCC GAGCCTGGCA 3800
TCATCGTGGCT GGGGCAGCCC CTGCCTCAGCT GCTGTCTCTG CCCGTGACCT 3850
TGAAGCCACCC TCCCCCCGTA CAGTTTTCCA TTCTCCTGGC TACTAGTGTG 3900
GCTGTTCATTG CCTACCTTGA TGAGTAGATT TCAGCCCTCC TAAAGCTGGG 3950
GCCTTTCCTCG TGCC 3964

(2) INFORMATION FOR SEQ ID NO: 1:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 676
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: mouse
(ix) FEATURE: Huntingtin-interacting protein -mHIP1a
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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Met Asn Ser Ile Lys Asn Val Pro Ala Arg Val Leu Ser Arg Arg
                  5                  10                  15

Pro Gly His Ser Leu Glu Ala Glu Arg Glu Gln Phe Asp Lys Thr
             20                  25                  30

Gln Ala Ile Ser Ile Ser Lys Ala Ile Asn Ser Glu Glu Ala Pro
         35                  40                  45

Val Lys Glu Lys His Ala Arg Arg Ile Ile Leu Gly Thr His His
     50                  55                  60

Glu Lys Gly Ala Phe Thr Phe Trp Ser Tyr Ala Ile Gly Leu Pro
 65                  70                  75

Leu Ser Ser Ser Ser Ile Leu Ser Trp Lys Phe Cys His Val Leu
             80                  85                  90

His Lys Val Leu Arg Asp Gly His Pro Asn Val Leu His Asp Tyr
         95                 100                 105

Gln Arg Tyr Arg Ser Asn Ile Arg Glu Ile Gly Asp Leu Trp Gly
    110                 115                 120

His Leu Arg Asp Gln Tyr Gly His Leu Val Asn Ile Tyr Thr Lys
125                 130                 135

Leu Leu Leu Thr Lys Ile Ser Phe His Leu Lys His Pro Gln Phe
            140                 145                 150

Pro Ala Gly Leu Glu Val Thr Asp Glu Val Leu Glu Lys Ala Ala
        155                 160                 165

Gly Thr Asp Val Asn Asn Ile Phe Gln Leu Thr Val Glu Met Phe
    170                 175                 180

Asp Tyr Met Asp Cys Glu Leu Lys Leu Ser Glu Ser Val Phe Arg
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185 190 195

Gln Leu Asn Thr Ala Ile Ala Val Ser Gln Met Ser Ser Gly Gln
200 205 210

Cys Arg Leu Ala Pro Leu Ile Gln Val Ile Gln Asp Cys Ser His
215 220 225

Leu Tyr His Tyr Thr Val Lys Leu Met Phe Lys Leu His Ser Cys
230 235 240

Leu Pro Ala Asp Thr Leu Gln Gly His Arg Asp Arg Phe His Glu
245 250 255

Gln Phe His Ser Leu Lys Asn Phe Phe Arg Arg Ala Ser Asp Met
260 265 270

Leu Tyr Phe Lys Arg Leu Ile Gln Ile Pro Arg Leu Pro Glu Gly
275 280 285

Pro Pro Asn Phe Leu Arg Ala Ser Ala Leu Ala Glu His Ile Lys
290 295 300

Pro Val Val Val Ile Pro Glu Glu Ala Pro Glu Glu Glu Glu Pro
305 310 315

Glu Asn Leu Ile Glu Ile Ser Ser Ala Pro Pro Ala Gly Glu Pro
320 325 330

Val Val Val Ala Asp Leu Phe Asp Gln Thr Phe Gly Pro Pro Asn
335 340 345

Gly Ser Met Lys Asp Asp Arg Asp Leu Gln Ile Glu Asn Leu Lys
350 355 360

Arg Glu Val Glu Thr Leu Arg Ala Glu Leu Glu Lys Ile Lys Met
365 370 375

Glu Ala Gln Arg Tyr Ile Ser Gln Leu Lys Gly Gln Val Asn Gly
380 385 390

Leu Glu Ala Glu Leu Glu Glu Gln Arg Lys Gln Lys Gln Lys Ala
395 400 405

Leu Val Asp Asn Glu Gln Leu Arg His Glu Leu Ala Gln Leu Lys
410 415 420

Ala Leu Gln Leu Glu Gly Ala Arg Asn Gln Gly Leu Arg Glu Glu
425 430 435

Ala Glu Arg Lys Ala Ser Ala Thr Glu Ala Arg Tyr Ser Lys Leu

440 445 450

Lys Glu Lys His Ser Glu Leu Ile Asn Thr His Ala Glu Leu Leu
455 460 465

Arg Lys Asn Ala Asp Thr Ala Lys Gln Leu Thr Val Thr Gln Gln
470 475 480

Ser Gln Glu Glu Val Ala Arg Val Lys Glu Gln Leu Ala Phe Gln
485 490 495

Met Glu Gln Ala Lys Arg Glu Ser Glu Met Lys Met Glu Glu Gln
500 505 510

Ser Asp Gln Leu Glu Lys Leu Lys Arg Glu Leu Ala Ala Arg Ala
515 520 525

Gly Glu Leu Ala Arg Ala Gln Glu Ala Leu Ser Arg Thr Glu Gln
530 535 540

Ser Gly Ser Glu Leu Ser Ser Arg Leu Asp Thr Leu Asn Ala Glu
545 550 555

Lys Glu Ala Leu Ser Gly Val Val Arg Gln Arg Glu Ala Glu Leu
560 565 570

Leu Ala Ala Gln Ser Leu Val Arg Glu Lys Glu Glu Ala Leu Ser
575 580 585

Gln Glu Gln Gln Arg Ser Ser Gln Glu Lys Gly Glu Leu Arg Gly
590 595 600

Gln Leu Ala Glu Lys Glu Ser Gln Glu Gln Gly Leu Arg Gln Lys
605 610 615

Leu Leu Asp Glu Gln Leu Ala Val Leu Arg Ser Ala Ala Ala Glu
620 625 630

Ala Glu Ala Ile Leu Gln Asp Ala Val Ser Lys Leu Asp Asp Pro
635 640 645

Leu His Leu Arg Cys Thr Ser Ser Pro Asp Tyr Leu Val Ser Arg
650 655 660

Ala Gln Ala Ala Leu Asp Ser Val Ser Gly Leu Glu Gln Gly His
665 670 675

Thr Gln Tyr Leu Ala Ser Ser Glu Asp Ala Ser Ala Leu Val Ala
680 685 690

Ala Leu Thr Arg Phe Ser His Leu Ala Ala Asp Thr Ile Val Asn

695 700 705

Gly Ala Ala Thr Ser His Leu Ala Pro Thr Asp Pro Ala Asp Arg
710 715 720

Leu Met Asp Thr Cys Arg Glu Cys Gly Ala Arg Ala Leu Glu Leu
725 730 735

Val Gly Gln Leu Glu Asp Gln Thr Val Leu Arg Arg Ala Glu Pro
740 745 750

Ser Leu Met Arg Ala Pro Leu Gln Gly Ile Leu Gln Leu Gly Gln
755 760 765

Asp Leu Lys Pro Lys Ser Leu Asp Val Arg Gln Glu Glu Leu Gly
770 775 780

Ala Met Val Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu
785 790 795

Asp Ala Val Arg Arg Ile Glu Asp Met Met Ser Gln Ala Arg His
800 805 810

Glu Ser Ser Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Asn
815 820 825

Ser Cys Thr Asp Leu Met Lys Ala Ile Arg Leu Leu Val Met Thr
830 835 840

Ser Thr Ser Leu Gln Lys Glu Ile Val Glu Ser Gly Arg Gly Ala
845 850 855

Ala Thr Gln Gln Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu
860 865 870

Gly Leu Ile Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Gln
875 880 885

Leu Val Glu Ser Ala Asp Lys Val Val Leu His Met Gly Lys Tyr
890 895 900

Glu Glu Leu Ile Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala
905 910 915

Gln Leu Val Ala Ala Ser Lys Val Lys Ala Asn Lys Asn Ser Pro
920 925 930

His Leu Ser Arg Leu Gln Glu Cys Ser Arg Thr Val Asn Glu Arg
935 940 945

Ala Ala Asn Val Val Ala Ser Thr Lys Ser Gly Gln Glu Gln Ile

950 955 960

Glu Asp Arg Asp Thr Met Asp Phe Ser Gly Leu Ser Leu Ile Lys
965 970 975

Leu Lys Lys Gln Glu Met Glu Thr Gln Val Arg Val Leu Glu Leu
980 985 990

Glu Lys Thr Leu Glu Ala Glu Arg Val Arg Leu Gly Glu Leu Arg
995 1100 1105

Lys Gln His Tyr Val Leu Ala Gly Gly Met Gly Thr Pro Ser Glu
1110 1115 1120

Glu Glu Pro Ser Arg Pro Ser Pro Ala Pro Arg Ser Gly Ala Thr
1125 1130 1135

Lys Lys Pro Pro Leu Ala Gln Lys Pro Ser Ile Ala Pro Arg Thr
1140 1145 1150

Asp Asn Gln Leu Asp Lys Lys Asp Gly Val Tyr Pro Ala Gln Leu
1155 1160 1165

Val Asn Tyr

(2) INFORMATION FOR SEQ ID NO:12:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 12:
GAAGATACCC CACCAAAC 18

(2) INFORMATION FOR SEQ ID NO:13:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 35
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other DNA
(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 13:
GCTTGACAGT GTAGTCATAA AGGTGGCTGC AGTCC 35

(2) INFORMATION FOR SEQ ID NO:14:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 14:
GGACATGTCC AGGGAGTTGA ATAC 24

(2) INFORMATION FOR SEQ ID NO:15:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: other nucleic acid
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: yes
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 15:
CUACUACUAC UACUAGGCCA CGCGTCGACT AGTACGGGII GGGIGGGII G 41

(2) INFORMATION FOR SEQ ID NO:16:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 516
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human

(x) FEATURE: exon 1 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 16:

```
TCTGTGGAAG GTTTGGAGGG GAGAGAGGGG CAGCTGGATG CTCTTGGGCC ACGGTCGCCC    60
CTGATCTCTC CGCCTCTTCC TCCTGCTCCG GGAGAAATAA TGTTTCCCTG GGGGATGAAA   120
GCATCTCTTT GTGCGGGCTT TAATTGCCAT GTTGTTGTGC CAAGGGAGTG AGTGGCGGCG   180
GGACCAGCAG CTGGCCACAG CCAATCCCNG CCAGTGCTCC CCAGTCCCTC ACCACCCCCA   240
GCCNGCTGGC TCCTGGGAGC GCTGCCCACC TCTGCCCCCA GCTGGGCGCC TGCAAGGAAC   300
CGACCACCCG TGGGGCTGGG GCACCTTGGC TGGAGCAGGA GAAAGGGGCG GCCTCTGGGA   360
GGGTCTCAGC CACTCTCAGA GGCTTATTCA TCTCATCCTC CTTTCCCTCC CCCTTCTTGT   420
TTTTCAGACT GTCAGCATCA ATAAGGCCAT TAATACGCAG GAAGTGGCTG TAAAGGAAAA   480
ACACCCCAGA AATATCCTTT GGATGTTGCT TGGAAG                              516
```

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 193

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exon 2 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 17:

```
TGTTTTCCAT AACCCCCCCT CACCGTGCAT ACTGGGCACC CACCATGAGA AAGGGGCACA    60
GACCTTCTGC TCTGTTGTCA ACCGCCTGCC TCTGTCTAGC AACCCAGTGC TCTCCTGCAA   120
GTTCTGCCAT GTGTTCCACA AACTCGTCCC AGATGGACAC CCGAACGTGA GTTCCTGGGG   180
CTATGGCGTG GCA                                                     193
```

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 104

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exon 3 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 18:

```
GTGTTCTTTG GCCCCTGCAG CTCCTGAAGG ACTCTCTGAG ATACAGAAAT GAATTGAGTG    60
ACATGAGCAG GATGTGGGTG AGTTTGGAGA TGTACTCAGG AGCC                    104
```

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 327
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 4 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 20:

```
AATTCCTGGC TCCAGATCTC TTGACTGTTA TGTTCTTCTT CTTCACTCTC TTTCCCCTCC    60
TCTTCCTAAA AGGGCCACCT GAGCGAGGGG TATGGCCAGC TGTGCAGCAT CTACCTGAAA   120
CTGCTAAGAA CCAAGATCCA GTACCACACC AAAGTGACTC TCTCCGCACA GTTCTCCCTC   180
CACCGCCGCC TCCCCTGCTC CATCCCTTCA GCCCCTCCCT GGGCTCATTT GTCAGCTCTT   240
TCAGGTAATA GACAGCCCAC CCTTCTGAGC AAGTCTCCAC ATCATCTACC CAAGCTGTCA   300
GAGAGCAAAG CCACCGCCAG GCCCACG                                       327
```

(2) INFORMATION FOR SEQ ID NO:21:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 331
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 5 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 21:

```
GGGCTCAAGC AATCCTCCCA CCTCGGCCTC CCAAGTAGCT GGGACCACAG GCGTGTGCCA    60
CCACGCCCGG CTGAGAGAGG GCGCTTCATG TCTTCTGCCC TGACTCCCTT CCTCTCCCTC   120
CCTTCCAGAA TCCCACCTTC CCAGGCAACC TGCAGATGAG TGACCGCCAG CTGGACGAGG   180
CTCGAGAAAG TGACGTGAAC AACTTGTAAG TGGCTCCTGC CCTGAGCCCA GGGAGGGAGA   240
AAGCTTTTGT GAATGCTGAC ACTTCTCATA ACCCTCATCC ACCCCCTGAT GGGGGGAGGC   300
CGTGGCTGGG ATCCCCACCA AAGCCCCTGG G                                  331
```

(2) INFORMATION FOR SEQ ID NO:22:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 470
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 6 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 22:

```
ACTGTCGCTG TCACTGTTGA CTTCACCAGG CTGCATGGCC ATAATACCCA CAAGGCTAAG      60
ACTTGGAGCT GGAGTTCTCT GTGTCTTTGC GCATCCACAT GAGCATTGGA GACTGGAGTA     120
GCGTAGAGCG TGGGGGAGGG GACAGGTAAC AGACCGGCCT CAGGCTGTGG AGTGTAAGCT     180
CTCTTTCCTC TTGGGTCCAG TTTCCAGTTA ACAGTGGAGA TGTTTGACTA CCTGGAGTGT     240
CAACTCAACC TCTTCCAAAC AGGTGAGTCT CTTCCCTCCC GTCTAACCCA GGCTCTCATG     300
GGAACTACCT AATTCCTAGT CCTCCTCTCC CTGCAAAGTG TGCAGCACAA GGGGTAGGAA     360
AATCCAGACA TTCACACCCC ATCTCTGGTC TCTCCAACCC TCGTGCAGGG AGGGACTGAA     420
CCTCTTCAGT ATTTTTCTTT TTAAGAGACA AGGTCTCGGC CGGGTGCAGT                470
```

(2) INFORMATION FOR SEQ ID NO:23:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 565
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 7 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 23:

```
TCTTCACCTG TTTAATGGGG ATACCTTTAC CTATCTCATG GGAGTGTTGT GAAGGTTAAA      60
TGAATTAGAT GAGGTAAAGC ACGCACAGAA TGGGTCCTTG GTGTATGTTG GAGCCCTGCC     120
TCTGCCCCTC TGAAGACCCC CCCTCTAATC CCCTGGCTCT ACCACCTTTC TCCCTCACTT     180
TTATTTCCTA GTATTCAACT CCCTGGACAT GTCCCGCTCT GTGTCCGTGA CGGCAGCAGC     240
GCAGTGCCGC CTCGCCCCGC TGATCCAGCT CATCTTGGAC TGCAGCCACC TTTATGACTA     300
CACTCTCAAG CTTCTCTTCA AACTCCACTC CTGTGAGTAC CGCGGGCCAG ATCTTCTTAC     360
ATGAGATTCA GGCCAGAGGG AGGATCCCAG CCTGAGGATG TCCCCAGACA AACCCAGTCC     420
TTCTCAGTGC CTTTGCCTGT CTGCTTCTCT TCCAAAAGGC CCCGGAGCTT CTGACCATTG     480
TGACCATAAA AGAGCAGGGC CCAGGCTTTG GTGACCCCAG TAAAGCCCCT GGCTTGCCAC     540
TCTTGCGTCC AGTGTTACAG GATCT                                           565
```

(2) INFORMATION FOR SEQ ID NO:24:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 233
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 8 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 24:

```
GGGACAGCTC TACCCCACTC GTCCCCCCTC GCACTGCTGG CCACATGCCC CAGGGTAGCT     60
GGGCCCCTCC CCCTCGAGAG CCCCGCTGTG GCTTCCCTGC CCTCTGGTCC CCCTCCCCTC    120
TCACACTCTT TCCAATTTCT TCCACCCCTC GCAGCTGACA CCCTGCAAGG CCACCGGGAC    180
CGCTTCATGG AGCAGTTTAC AAAGTAAGTG GTTCAAGTAA CAGGATTGGA GGT           233
```

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 578

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exons 9 and 10 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 25:

```
TGAATCCCAG CACCATGGAG TTTATCTCCT TGACACCCTC TGCCTTTGGC CTGGCCACCC     60
GGCAGCAAAG CCAGGTGGCT GCTCTGTCCC CTACATGGGG CTGATGAAGA CACCCAGCAC    120
CCCTCAGGTC CTTCTCCACC CCTAGGTTGA AAGATCTGTT CTACCGCTCC AGCAACCTCC    180
AGTACTTCAA GCGGCTCATT CAGATCCCCC AGCTGCCTGA GGTAAGCATG CCCAACCACA    240
CACCCTCGGC ACTGCAGAGG CCCCAGGTAC TCTCTTAAGG GCCCGCCCCC CCTCCCAAGC    300
AAGCACTATT TGAGGATNTG TCTCCGTCTT CAGAACCCAC CCAACTTCCT GCGAGCCTCA    360
GCCCTGTCAG AACATATCAG CCCTGTGGTG GTGATCCCTG CAGAGGCCTC ATCCCCCCAC    420
AGCGAGCCAG TCCTAGACAA CCATCACCTC ATGGACATNG ATGCCTCTCA GCAGGTGAGG    480
ACCACTTCCC AGAGAAACTT GGCCTTTCCT CTCACCTGCA AGTACAGGGG AGAGGCTGGG    540
GGAGACCCTG GCCAAAGCCC ATTGACTCTA ACCAGCTT                            578
```

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 390

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii)MOLECULE TYPE: genomic DNA

(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:

(A) ORGANISM: human

(x) FEATURE: exon 11 of HIP1

(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 26:

```
AAAAAAATTT AAAAAATTAA ACAGGTCTGA ACCCTTTAAT TCGAGAAAGC GGGCATTCTC     60
CCATATCACT CAACTGNGCC ACACACAGAA TTCTCTGGCT CTCTGACTTA TTCTCACTCC    120
TTTTTGGTCA ACCACAGAAT TTATTTGACA ACAAGTTTGA TGACATCTTT CCCAGTTCAT    180
TCAGCAGTGA TCCCTTCAAT TTCAACAGTC AAAATGCTCT CAACAAGGAT GAGAAGTGAG    240
TCCAAGCTGG GTTCAAGCAC ATCCTTCAGG AGCTAAGTTA AGCCATGGTC TGCCTCAAAA    300
CACTAACCAA AGAGGAATTC TTAATGATAC TGGGGCTTCT TAGATACAGA ACATCTTCAA    360
GGGTTGGGGG CAATGGCTTA TGCCTGTAAT                                     390
```

(2) INFORMATION FOR SEQ ID NO:27:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 547
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 12 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 27:

```
AAAATCAATA ACCATGGATT TATGAGTATT AGATTAGTAT CTGGTAACAT TTAGAGTATA     60
ATTTATGGCA TTTCAAACAA TTGTCCCCAA ATTAATACCA GCTTTTAATT TCCTGCCCTG    120
AGCTCACAAT TAAAAACAGA GGGATAGAAG CACTATGAAA GCAAACTCAT TCCCCTTCTC    180
TTCCCAGGGA CCACTTAATT GAGCGACTAT ACAGAGAGAT CACTGGATTC AAGCCACAGC    240
TAGAAAACAT GAAGACTGAG GTATAACTTG GATCTGCTCT GCCTTTGCGC TTCACCAAAA    300
CAGGGTAGAT TTGAATCTTA AATTGGCATC ACACTAGCCA CGCCACACTG CTCACACCTG    360
TAATCCTAGC ACTTTGGGAG GCCAAGGCAG GAGGATTACC TGAGGTCGGG AGTTCGAGAC    420
CAGCCTGGGC AACAGGGTGA AACCCCGGTC TTCAATAAAA ATGCAATAAT TAGCCGGGTG    480
TGTTGGCAGG CACCTCTAAT CCCAGCTACT CGGGAAGCTG AGGCATGAGA ATTGCTTGAA    540
CTTGGGA                                                              547
```

(2) INFORMATION FOR SEQ ID NO:28:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 436
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 13 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 28:

```
CCCCCAGCCA CTCTAAAGAG GACCACAATT CCCCGGCCAT CATCCCCTGT TATTGTTGTT     60
GATTGAGGGG CTCCTAATGA CCAGATGGTC CAACCCTCCT CCCACCTGCA GAGTTGACTT    120
AGGGGAATCA GGTATTTACT TGGAAGCATG GTAGGACCCG CTTCTCCGGC CCATGCCCGT    180
GACCCGTGGC AGTGGGCGGT TGGCCTCATG ACCGGAGTCC CCCCACAGAG CCAGCGGGTT    240
GTGCTGCAGC TGAAGGGCCA CGTCAGCGAG CTGCAAGCAC ATCTCCCCCA GCAGCAGCAC    300
CTGCGGCAGC ACCCCCCCCA CGACTGTGAA TTCCTGCGGG CAGAACTGGA CGAGCTCAGG    360
AGGCAGCGGG AGGACACCGA GAAGGCTCAG CGGAGCCTGT CTGACATAGA AAGNCAGCCC    420
TGGGTGGGGG CGGGGG                                                    436
```

(2) INFORMATION FOR SEQ ID NO:29:
(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 469
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 14 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 29:

```
GACTTGAGCC CAAGGAGGTC AAGGCTGCAG TGAACAGTGA TTGTGCCACT GCACCCCAGC      60
CTGGGTGACA GAGCAAGACT GTCTCAAAAC AAAACAAGGA GGACCTTCTA GGGACCCTGG     120
CTCATTGCAA GGAAGGCAAG GGTCCCTGCT AGCTTAGACT CCTCACGTTC GTCCTTTACA     180
ATACAGGGAA AGCTCAAGCC AATGAACAGC GATATAGCAA GCTAAAGGAG AAGTACAGCG     240
AGCTGGTTCA GAACCACGCT GACCTGCTGC GGAAGGTAAG ACCCTCAGCC CCTGTCACCA     300
TCCTGCAGCC CCTCCACCTC TAGGGAGACA GCGGCTCAGG CCTGTGGCTT CCCCGGGGCC     360
AGCAACCCCT ACATTGATCT CTAAGGCATT GCCGTCATCT CGGGAACCAC ACCTTTTCAG     420
GCTTCCTTGC CTCTGTGTCT TGGGCTGTGT CCTGCGTCCC AATCCCATC                 469
```

(2) INFORMATION FOR SEQ ID NO:30:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 359
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 15 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 30:

```
CGGTAGGAAA GTGATTCCTG TGTCTGACTC TAGGGCACCC ACAGCCTCAG TATGATTGTC      60
CTAGAAGGAG GATGTCCTCT AACCCTCCCA TCTCCTGGTT CAAGACACTG TTCTTCTTTT     120
GCAGAATCCA CACCTGACCA AACAGGTGTC CATGGCCAGA CAAGCCAGG TAGATTTCCA     180
ACGAGAGAAA AAAGAGCTGG AGGATTCGTT GGAGCGCATC AGTGACCAGG GCCAGCGGAA     240
GGTGAGTGGG ACGAGGAGCA CTCCGCAAAT GAGGGAGGGG GCTGTTGAGT TGGTGGCGGG     300
GGCTTTGTGG CCTTCTGCTC CATGGGCAGT TCTGTGGGTC GGTGGCATC ACACAGCAG       359
```

(2) INFORMATION FOR SEQ ID NO:31:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 209
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no

(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 16 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 31:

```
GTTGATCGCT TGGGACGTTT TTACATTTTT ATATTCTTTG TCACTGTCAC CCAGATCAGA      60
GTCCCTCTGT TTTTCTTCTC TTTCAGACTC AAGAACAGCT GGAAGTTCTA GAGAGCTTGA     120
AGCAGGAACT TGCCACAAGC CAACGGGAGC TTCAGGTTCT GCAAGGCAGC CTGGAAACTT     180
CTGCCCAGGT AAATACCTCC TTTTTTTTT                                       209
```

(2) INFORMATION FOR SEQ ID NO:32:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 485
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 17 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 32:

```
CCCCCACTGC AATCAGTGTG TCCCCGGGAG GGAATCAGAG TGGCAGGTTA AAGACCCATC      60
ACCTTCCCAG TCCTTGCAAC CCGGTGGTGC CTTCCACCTC TGGGAAGTAG GGACTGTTTA     120
ACTCAACCAG CGTCTCCCTC TTTCCTTGTG GTCACCTTTG CAGTCAGAAG CAAACTCGCC     180
AGCCCACTTC GCCGAGCTAG AGAAGGACCC CCACACCCTC CTCAGTGGCG CAGCTCATAG     240
GGAGGAGGAA TTATCTGCTC TTCGGAAAGA ACTGCAGGAC ACTCAGCTCA AACTGCCCAC     300
CACAGACGGT CACGGACATG GACACGAGCG ACCACCTGTC AATTCCCACC GAGGGCCTCT     360
CCGCATGCAC GGAGGCTGGG ACCACCCCGG GGCTGCTGAG AAGGGGTTTG GGGCCTTGGC     420
CTGATTGTGC ACACATTCTG TAGGTGTAAT GCCAGCAGGC CCTGCATTGC CTGCACAGTC     480
CATGA                                                                485
```

(2) INFORMATION FOR SEQ ID NO:33:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 468
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 18 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 33:

```
TTACTGGCTT GGACCTCATT GGCCATGACT TGAGCTAAGA TGCTAAGAGC CCCAGCCAGG      60
TCATCCTGCT CAGGTTCATT ATGGAGTCTA GGGCAGACTC TCACCTCCCT GGACCATTTT     120
```

TAGAATCTAT GTGCCAGCTT GCCAAACACC AACGAAAAAT GCTTCTGGTG GGGTCCAGGA 180
AGGCTCCGGA GCAGGTGATA CAAGACGCCC TGAACCAGCT TGAAGAACCT CCTCTCATCA 240
GCTGCGCTGG GTCTGCAGGT ACACTTGCAA TTGCCCACCT GGCAGGGGCC AGGTCCTTAC 300
AGCCTGAGAC TCTGTTGATG TTGAATCTCA TGTGAGACTT AGCTCAGGGG CTCTCAGCCC 360
AGCAGCATGT CAGCATTACC TTAGGGGCCC CCAGGCCCCA TCCTAGATCA GTTACATGTG 420
GAAACTCTGT GCATTAGTGC CTATACACTA GTATTTTAGT ATTTTCCT 468

(2) INFORMATION FOR SEQ ID NO:34:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 393
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 19 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 34:
CACTAGTAAG CTCCTCCATT CAGTGCTTAA TTAACGAGGA TGAAGCCAGC TATCAGAACT 60
TGCTCTGACC TTGCCCTGTG TTCCCTCTCA CAGATCACCT CCTCTCCACG GTCACATCCA 120
TTTCCAGCTG CATCCACCAA CTGGAGAAAA GCTGGAGCCA GTACCTGCCC TCCCCAGAAG 180
GTAAGAATGG CCAAGGACAG TCTCTGTCGG CTACTGATGG CCAGACAGGG TTCAGAAGCA 240
CCTGAATGCG GGGATAGTGA CAGGTCCCTC TGCATCAAGA AAGGCATGTA CCCAACTCAT 300
ACAAGAAAGG CATCTAGGCA ACTCATAAAA CGGGAGGACA GCCTATGAAA GTGTCACCAT 360
CAACCAGACC TGAGAAACTT CTCTTTCCAA TCC 393

(2) INFORMATION FOR SEQ ID NO:35:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 421
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 20 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 35:
GGCCTGCCCA GAAGGTAAGA AGGCCCAAGG ACAGTCTCTG TCGGCTAGTG ATGGCCAGAC 60
AGGGTTCAGA AGCACCTCAA TGCGGGGATA GTGACAGGTC CCTCTGCATC AAGAAAGGCA 120
TGTAGGCAAC TCATACAAGA AAGGCATGTA CGCAACTCAT AAAACGGGAG GAGAGGCTAT 180
CAAAGTGTCA CCATCAACCA GACCTGAGAA ACTTCTCTTT CCAATCCTGC CACACATCAG 240
TGGACTTCTC CATTCCATAA CCCTGCTGGC CCACTTGACC ACCCACGCCA TTGCTCATGG 300
TGCCACCACC TGCCTCAGAG CCCCACCTGA CCCTGCCGAC TGTGAGTACT GGGCCATGAC 360
GGGCTGTTCA TGGACCAGGG GACCACCCCG CCTTTAAAAG TCTCTGTTCC GCCGGGCGCA 420
G 421

(2) INFORMATION FOR SEQ ID NO:36:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 498
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 21 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 36:

```
AGGCCCAGGC AGGAGAATCG CTTGAACTCA GGAGGCGGAG TTTGCAGTGA GCCGAGATGG      60
CGCCACTGCA CTCCAGCCTG GGCAACAAGA GCGAGACTCC ATCTCAAAAA AAAACTGTCT     120
ATTGCCTTGT ATCTCCAGCA CTGACCGAGG CCTGTAAGCA GTATGGCAGG GAAACCCTCG     180
CCTACCTGGC CTCCCTCCAG GAAGAGGGAA GCCTTGAGAA TGCCGACAGC ACAGCCATCA     240
GGAACTGCCC GAGCAAGATC AAGGCCATCG GCGACGTTAC TGGAGTAGTA TCATTGAGGA     300
GCATTGTTAT TCTTCTGCCT GTGCGTGCTG GTGAATGGCC AGGGAATCGG TGATGTTCTC     360
AGCTAGTTCT TTCTGCACTT AGAACTTGAT TCTACAAAGA CATTGTTAAA ATTGGAAAAT     420
CTGCCCGGGT GCAGTGATTT ATGCCTGTAA TCCCAGCACT TTGGGAGGCC GAGTCAGGAG     480
GATCACTTGA GGCTAGAC                                                   498
```

(2) INFORMATION FOR SEQ ID NO:37:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 427
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 22 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 37:

```
CCCTGTGGCT TGCAGAAGGT GTTTGCTGGG TGGCCTCCTG CCTTGCCATC TTGTAAGCGT      60
TACAGATGGC AGAGGAGAAG AGACAGGAGG CCCCAAGGTC AGTTCAGCCT TTGTGATGTG     120
TTCACAGGAG CTCCTGCCCA GGGGACTGGA CATCAAGCAC GAGGAGCTGG GGGACCTGGT     180
GGACAAGGAG ATGGCGGCCA CTTCAGCTGC TATTGAAACT GCCACGGCCA GAATACAGGT     240
AGGAGGTTCC TGCAGGATCT CCTGAAACGA TGCCTTTGCA GCTGCCCTTC TGCAACACTG     300
CTCATTAAAC ATGTCACAGT CGTTCATTAA GGCCAAGGCA ACCCCCTAAG ACAGAAACCA     360
GAATTTGCCA GGCACAGTGG CTCATGCCTG TAACCCCAGC ACCTTGGGAG GATCACTTGA     420
GTCCAGG                                                               427
```

(2) INFORMATION FOR SEQ ID NO:38:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 367

(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 23 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 38:

```
CCCCCTGAAT AGTTTAGAGT CTGGATTCTT TTCTGACTCT CTCAAGAATG TGGGCAGGGA      60
CTTGGGGACT TCCAGATTCA GGTTTCCCAG CTACCACAGC ATGTTGGACT GAAAGTATAG     120
TAAGACATTA GTCCATGCTT AATATTCAAG GCACATTTAG AAACCATGCT TCTTTTTCAC     180
AGGAGATGCT CAGCAAATCC CGAGCAGGAG ACACACGCAT CAAATTGGAG GTGAATGAAA     240
GGTCGGTCTG AGCGGCATTC TGGGACCTAG GGGAGCAGGA TCTGTCTTCC TGACATTGGT     300
CTATACTTTC CATACTTATT AGGGAATTAG AGGAGAGCAG TACCACCCAC CCCCAACCCC     360
TGAGTTG                                                               367
```

(2) INFORMATION FOR SEQ ID NO:39:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 502
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 24 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 39:

```
CCCCGCAGAA TCTTCCAGCA ACCTCAGCAC CCTTCTTACC TCCCTTTCCC ATTCCAAGCT      60
TGCCTTTGGC TAGGAGTGGG GAAGAGAACC GTCGTGTTCA TTGATCTTGG AGCTTGATCT     120
CAGTGTATCC TCGACTTCTT TGTTTGGCAG GATCCTTGCT TCCTGTACCA GCCTCATGCA     180
AGCTATTCAC GTGCTCATCG TGGCCTCTAA GGACCTCCAG AGAGAGATTG TGGAGAGCGC     240
CAGCGTGAGC GTGGGTGTGG GCCCTGGGCA GGAAGAGGAG GCATCGGTGA CAGACTCCCG     300
CTCCAACGGA CTCTGTCATG CTGCCGTCTT ACTCTGTGTC TCCACCTGAG TACAGAGCAG     360
CCACTCCTCT AGATATCAGC AGAGGCCCTC CGCAGAAGTC AGAGCTCCAG GACCTCCCCA     420
GAGGGTGGCC AGGCATGTGT CCCAACTCCA GCTCCCTTCG CACAGGCACA CATTGTTGGA     480
ACTTGCTGTG GCAGCCCTTT TT                                               502
```

(2) INFORMATION FOR SEQ ID NO:40:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 437
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no

(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 25 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 40:

```
TTTTGGTCTC TGAATCTTCT TCTTTTTTGT AAAATGGGAA TACTAATGCT TATGTCTCAG      60
AGTTACTATG AGGATGATTT GGGATAATAT ATGTATAAAA GCACCTGCCA TATAGTACAT     120
GCTCAATAAA AGGTGGCTAT TACTATTTTT TATTTCCCTA GGGTACAGCA TCCCCTAAAG     180
AGTTTTATGC CAAGAACTCT CCATGGACAG AACCACTTAT GTCAGCCTCC AAGGCTGTGG     240
GCTGGGGAGC CACTGTCATG GTGTAAGTAT CTATTGGTAC CAAGGGTCCT CCCATGACCC     300
CTCTTCCATT GATCCACTCC AAACAATACC TAACCAGCCA AAAAAAAATC TGTCCCTTAG     360
AAATAAACTA TTGATCAGGA AGTCAATAGG ACCGAGTTTA CAAGGGAGCC TGGCTCTCCC     420
AGGGGACACA GGGCAGG                                                    437
```

(2) INFORMATION FOR SEQ ID NO:41:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 351
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 26 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 41:

```
GGGAGCCCTGG CTCTCCCAGG GGACACAGGG CAGGCAGCCT CCCCTCCCTG TTTAGCCAAG      60
GGCGATGGGG TGGTCTGGAG GTGCCATTGT GGAGGAGTTG CAGCTCATTT GCCCCTAACC     120
TAGTCCCTCT TCTCGTTTTC CATCAGGGAT GCAGCTGATC TGCTNGGTACA AGGCAGAGGG     180
AAATTTGAGG AGCTAATGGT GTGTTCTCAT GAAATTGCTG CTAGCACAGC CCAGCTTGTG     240
GCTGCATCCA AGGTAGGACC TGCCTGGACC TCCTAGGACG CTGGAAGGCC TGCTTAGAGA     300
GTACTAGGCT ACGTTAAAGA GTACTTGGCT GGGTTAGGCA CTNCTTGGCT G              351
```

(2) INFORMATION FOR SEQ ID NO:42:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 418
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 27 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 42:

```
CTTTTTATAT GATAGATATG TCAGGAGCTG ACTATACTCA GCAGATTTTG AGAAGCTGAT      60
TGGTGATTGC CGTTTGGCCC ACATATCTTT GCTAAGAACC ATCAGAGCAA TTATCTGATT     120
CAGTCCTTGT TGCTCTAGGT GTTGTATGAA CCTAAATCTG CTTTGTCCTG GTAGGTGAAA     180
```

GCTGATAAGG ACAGCCCCAA CCTAGCCCAG CTGCAGCAGG CCTCTCGGGG AGTGAACCAG 240
GCCACTGCCG GCGTTGTGGC CTCAACCATT TCCGCCAAAT CACAGATCCA NGAGACAGGT 300
AGCCTTTCCA AAGGGACCCT TTTCTTACCC ACCCTGTTGA GCTCTTCTCT GCATCCTTCC 360
CTGTGATCCC AACCAAATCC CACAGGACTG TGTCTAAATT CTTTCATATT TTTCATCT 418

(2) INFORMATION FOR SEQ ID NO:43:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 279
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 28 of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 43:
TTTCCACAGA GCATTGCCAT TGGCTGCCTC TCAGGTGCCA GTCAGCCAGC CTAGAATTTG 60
ATGAGACCTT CTTGTTTCCA TCCTTGCACA CAACATGGAC TTCTCAAGCA TGACGCTGAC 120
ACAGATCAAA CGCCAAGACA TGGATTCTCA GGTTAGGGTG CTAGAGCTAC AAAATGAATT 180
GCAGAACGAC CGTCAAAAAC TGGGACIACC TCGGAAAAAG CACTACGAGC TTGCTGGTGT 240
TGCTGAGGGC TGGGAAGAAG GTAAGCTGAC TCAAAGGAT 279

(2) INFORMATION FOR SEQ ID NO:44:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3715
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: genomic DNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(x) FEATURE: exon 29 and partial cds of HIP1
(xi)SEQUENCE DESCRIPTION: SEQ ID NO: 44:
AACATAAATT ATCATTGTCT TTTAGGAACA GAGGCATCTC CACCTACACT GCAAGAAGTG 60
GTAACCGAAA AAGAATAGAG CCAAACCAAC ACCCCATATG TCAGTGTAAA TCCTTGTTAC 120
CTATCTCGTG TGTCTTATTT CCCCAGCCAC AGGCCAAATC CTTGGAGTCC CAGGGGCAGC 180
CACACCACTG CCATTACCCA GTGCCGAGGA CATGCATGAC ACTTCCCAAA GACTCGCTCC 240
ATAGCGACAC CCTTTCTCTT TGGACCCATG GTCATCTCTG TTCTTTTCCC GCCTCCCTAG 300
TTAGCATCCA GGCTGGCCAG TGCTGCCCAT CAGCAAGCCT AGGTACGAAG AGGGGTGCTC 360
GGCGGCAGGG CCACTCAACA CAGAGGACCA ACATCCAGTC CTGCCGACTA TTTGACCCCC 420
ACAACAATGG GTATCCTTAA TAGAGGAGCT GCTTCTTCTT TCTTGACAGC TTGGAAAGGG 480
AAGATCTTAT GCCTTTTCTT TTCTGTTTTC TTCTCAGTCT TTTCAGTTTC ATCATTTCCA 540
CAAACTTGTG AGCATCAGAG CGCTGATGGA TTCCAAACCA GGACACTACC CTGAGATCTG 600
CACAGTCAGA AGGACGGCAG GAGTGTCCTG GCTCTCAATC CCAAAGCCAT TCTCCCCCTC 660
TTTGGGCAGT GCCATGGATT TCCACTGCTT CTTATGGTGG TTGGTTGGGT TTTTTGGTTT 720
TGTTTTTTTT TTTTAAGTTT CACTCACATA GCCAACTCTC CCAAAGCCCA CACCCCTGGG 780
GCTGAGTCTC CAGGGCCCCC CAACTGTGGT AGCTCCAGCG ATGGTGCTGC CCACGCCTCT 840

CGGTGCTCCA TCTCCGCCTC CACACTGACC AAGTGCTGGC CCACCCAGTC CATGCTCCAG 900
GGTCAGGCGG AGCTGCTGAG TGACAGCTTT CCTCAAAAAG CAGAAGGAGA GTGAGTGCCT 960
TTGCCTCCTA AAGCTGAATC CCGGCGGAAA GCCTCTGTCC GCCTTTACAA GGGAGAAGAC 1020
AACAGAAAGA GGGACAAGAG GGTTCACACA GCCCAGTTCC CGTGACGAGG CTCAAAAACT 1080
TGATCACATG CTTCAATGGA GCTGGTGAGA TCAACAACAC TACTTCCCTG CCGGAATGAA 1140
CTGTCCGTGA ATGGTCTCTG TCAAGCGGGC CGTCTCCCTT GGCCCAGAGA CGGAGTGTGG 1200
GAGTGATTCC CAACTCCTTT CTGCAGACGT CTGCCTTGGC ATCCTCTTGA ATAGGAAGAT 1260
CGTTCCACTT TCTACGCAAT TGACAAACCC GGAAGATCAG ATGCAATTGC TCCCATCAGG 1320
GAAGAACCCT ATACTTGCTT TCTCTACCCTT AGTATTTATT ACTAACCTCC CTTAAGCAGC 1380
AACAGCCTAC AAAGAGATGC TTGGAGCAAT CAGAACTTCA GGTGTGACTC TAGCAAAGCT 1440
CATCTTTCTG CCCGGCTACA TCACCCTTCA AGAATCAGAA GAAAGCCAAG GTGCTGGACT 1500
GTTACTGACT TGGATCCCAA AGCAAGGAGA TCATTTGGAG CTCTTGGGTC AGAGAAAATG 1560
AGAAAGGACA GAGCCAGCGG CTCCAACTCC TTTCAGCCAC ATGCCCCAGC CTCTCCCTGC 1620
CCTGTGGACA GGATGAGGAC ACAGGGCACA TGAACAGCTT GCCAGGGATG GGCAGCCCAA 1680
CAGCACTTTT CCTCTTCTAG ATGGACCCCA GCATTTAAGT GACCTTCTGA TCTTGGGAAA 1740
ACAGCGTCTT CCTTCTTTAT CTATACCAAC TCATTGGTGC TAGCCATCAA GCACTTCCCA 1800
GGATCTGCTC CAACAGATTA TTGCTAGGTT TTGCTACATG ACGGGTTGTG AGACTTCTGT 1860
TTGATCACTG TGAACCAACC CCCAICTGCC TAGCCCAGCC CCCTCCCCAA CTCCCTCTCT 1920
GTGCATTTTC TAAGTCGGAC ATTCAAAAAA CTCTCTCCCA GGACCTCGGA TGACCATACT 1980
CAGACGTGTG ACCTCCATAC TGGGTTAAGC AACTATCAGC ACTAGAAATT GGGCAGTCTT 2040
AATGTTGAAT GCTGCTTTCT GCTTAGTATT TTTTTGATTC AAGGCTCAGA AGGAAGGGTG 2100
CGTGGCTTCC CTGTCCCAGT TGTGGCAACT AAACCAATCC CTGTCTTTCTT GATGCGGGTC 2160
AACATTTCCA AAAGTGGCTA CTCCTCACTT CTAGATCTCA GCCATTCTAA CTCATATGTT 2220
CCCRATTACC AACCGGTGGC CGGGCACAGT GGCTCACGCC TGTAATCCCA GCACTTTGAC 2280
AGGCTGAGGT GGTAGGATCA CCTGAGGTCA GGAGTTCAAG ACCAGCCTGT CCAACATGGT 2340
GAAACCCCGA TCTCTACTAA AAATACCAAA AATTAGCCGA GCGTAGTGAC GGGTGCCTGT 2400
AATCCCAGCT ACTCAGGAGG CTGAGACAGG AGAATCACCT GAACCCCAGA GGCAGAGGTT 2460
GCAGTGAGCT GAGATCACGC CATTGTACTC CAGCCTGGGC AACAAGAGCA AAACTCCGTC 2520
TCAAAAAAAA AAAAAAATTA CAAATGGGGC AAACAGTCTA CTGTAATGGA TCAAATTAAG 2580
ATTCTCTGCC CAGCGGGGCA CACTGGCGCA TGCCTGTAAT CCCAGAACTT TGGGAGCCCA 2640
AGACGGGATG ATTGCTTGAG CTCAGGAGTT TGAGACCAGC CTGGGCATCA TAGCAAGACC 2700
TCATCTCTAC TAAAATTCAA AAACAAAATT AGCCGGGCAT GATGGTGCAT GCCTGTAGTC 2760
TCAGCTAGTT GGCCAGCTAA GGTGGGAGAA TAGCTTGAGC TTGCCAAGTC GAGGCTGCAG 2820
TCAGCCCTGA TTGTGCCAGT GCACTCCGGC CTGGGTGACA GAGTGAGACC CGTGCTCAAA 2880
AAAAAAAAGA TTCTGTGTGA GACCCCAGCC CAGGAGTTTG AGGCTGCAAT GAGCCATGAT 2940
TTCCCACTGC ACTCCAGCCT GAGTGACAGA GCGAGACTCC ATCTCTTTAA AAACAAACAA 3000
AAAATTATGT GAATGATCCT GTCTCTAAAA AGAAGCCACA GAAATGTTTA AAAACTTCAT 3060
CGACTTAGCC TGAGTCATAA CGGTTAAGAA AGCACTTAAA CAGAAGCAGA CGCTAATTCA 3120
GTGTCAGATC AGGAAGTAGC TGTCAGATGT CACATAATTA CTTTCGTAAT AGCTCAGATT 3180
AGAATGGCTA CCCCATTCTC TAGACAAAAT CAAATTGTCC TATTGTGACT CTTCTAAAAA 3240
TGAAGATGAA GAGCTATTTA ATGACACACC TTGCATTAAA ACGGGAATCA CATCTTAAAG 3300
CTAAAAATGA ACCTGCAACC CTTCTAAATG AGTCACTGAG CATCACTAGT CACAAGTCTC 3360
GGGTGAGCCT AAATGGGTCA TGACAAGATG GGACAGCAAC AAAATCATGG CTTAGGATCG 3420
ACAAGAAGTT AAAAAACAGC TGCATCTCTT ACTTAAGTTT GTAAGACAGT GCCCTGAGAC 3480
CTCTAGAGAA AAGATGTTTC TTTACATAAG AGAAAGAAGG CCAGACATGC TGTCTCACAC 3540
GTTTAATCCC AGCACTTTGG GAGGCAGGGG CGGGTGGATC ACCTGAGGTC AGGAGTTCAA 3600
GACTAGCCTG GCCAACATGG TGAAACCCCG TCTCTACTAA AAATACAAAA ATTAGCCGGC 3660
CATGGTGGCA GGCGCCTATA ATCCCAGCTA CTGGGGAGGC TGAGGCAGGA GAATC 3715

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Published
With international search report.

(88) Date of publication of the international search report:
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(54) Title: APOPTOSIS MODULATORS THAT INTERACT WITH THE HUNTINGTON'S DISEASE GENE

(57) Abstract

A family of proteins, including a specific human protein designated as HIP1, has been identified that interact differently with the gene product of a normal (16 CAG repeat) and an expanded (>44 CAG repeat) HD gene. Expression of the HIP1 protein was found to be enriched in the brain. Analysis of the sequence of the HIP1 protein indicated that it includes a death effector domain (DED), suggesting an apoptotic function. Thus, it appears that a normal function of Huntingtin may be to bind HIP1 and related apoptosis modulators, reducing its effectiveness in stimulating cell death. Since expanded huntingtin performs this function less well, there is an increase in HIP1–modulated cell death in individuals with an expanded repeat in the HD gene. This understanding of the likely role of huntingtin and HIP1 or related proteins (collectively "HIP–apoptosis modulating proteins") in the pathology of Huntington's disease offers several possibilities for therapy. First, because the function of huntingtin apparently depends at least in part on the ability to interact with HIP–apoptosis modulating proteins, added expression (e.g., via gene therapy) of normal (non–expanded) huntingtin or of the HIP–binding region of huntingtin should provide a therapeutic benefit. Other DED–interacting peptides could also be used to mask and reduce the interaction of HIP–apoptosis modulating proteins with the death signaling complex. Alternatively, a mutant form of HIP–protein from which the DED has been deleted might be introduced, for example using gene therapy techniques. Because HIP–apoptosis modulating proteins have been shown to self–associate, a protein with a deleted DED may compete with endogenous HIP–protein in the formation of these associations, thereby reducing the amount of apoptotically–active HIP–protein.

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UA	Ukraine
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US	United States of America
UZ	Uzbekistan
VN	Viet Nam
YU	Yugoslavia
ZW	Zimbabwe

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/11743

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :C07H 21/04; C12Q 1/68; C07K 5/00
US CL :536/23.5; 435/6; 530/350
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/23.5; 435/6; 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPAT, CAPLUS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WANKER et al., HIP-I: A Huntingtin Interacting Protein Isolated by the Yeast Two-hybrid System. Human Molecular Genetics. March 1997, Vol. 6, No. 3, pages 487-495, see entire document.	1-15

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
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"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 20 DECEMBER 1999	Date of mailing of the international search report 3 February 2000 (03.02.00)
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer SCOTT HOUTTEMAN Telephone No. (703) 308-0196